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RESPIRATORY CARE

A MONTHLY SCIENCE JOURNAL
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ORIGINAL CONTRIBUTIONS

Effects of Propofol on Rapid Shallow Breathing Index in Assessment for Ventilator Weaning

Comparison of Two Treatment Regimens for COPD Patients Hospitalized with Acute Exacerbations

Cumulative Dose-Response Study of Ipratropium Bromide Dry Powder Inhalation in COPD

CASE REPORTS

Churg-Strauss Syndrome Thirty Years After the Onset of Ulcerative Colitis

REVIEWS, OVERVIEWS, & UPDATES

Practical Management of Acute Asthma in Adults

GRAPHICS CORNER

Detection of Patient-Ventilator Asynchrony During Low Tidal Volume Ventilation

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DuoNeb can have a significant cardiovascular effect, significant hypokalemia and the potential life-threatening paradoxical bronchospasm. Caution is advised in patients with convulsive disorders, hyperthyroidism, diabetes mellitus, narrow-angle glaucoma, prostatic hypertrophy or bladder-neck obstruction. Co-administration of DuoNeb Inhalation Solution and other sympathomimetic agents may increase the risk of adverse cardiovascular effects.

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE

DuoNeb is indicated for the treatment of bronchospasm associated with COPD in patients requiring more than one bronchodilator

CONTRAINDICATIONS

DuoNeb is contraindicated in patients with a history of hypersensitivity to any of its components, or to atropine and its derivatives.

WARNINGS

Paradoxical Bronchospasm: In the clinical study of DuoNeb, paradoxical bronchospasm was not observed. However, paradoxical bronchospasm has been observed with both inhaled ipratropium bromide and albuterol products and can be life-threatening If this occurs, DuoNeb should be discontinued immediately and alternative therapy instituted

Do Not Exceed Recommended Dose: Fatalities have been reported in association with excessive use of inhaled products containing sympathomimetic amines and with the home use of nebulizers.

Cardiovascular Effect: DuoNeb, like other beta adrenergic agonists, can produce a clinically significant cardiovascular effect in some patients as measured by pulse rate, blood pressure, and/or symptoms. Although such effects are uncommon for DuoNeb at recommended doses, if they occur, the drug may need to be discontinued. In addition, beta agonists have been reported to produce ECG changes, such as flattening of the T-wave, prolongation of the QTc interval, and ST segment depression. The clinical significance of these findings is unknown Therefore, DuoNeb, like other sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

Immediate Hypersensitivity Reactions: Immediate hypersensitivity reactions to albuterol and/or ipratropium bromide may occur after the administration of DuoNeb as demonstrated by rare cases of urticaria, angioedema, rash, pruritus, oropharyngeal edema, bronchospasm, and anaphylaxis.

PRECAUTIONS

General

1 Effects Seen with Sympathomimetic Drugs. As with all products containing sympathomimetic amines, DuoNeb should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension, in patients with convulsive disorders, hyperthyroidism, or diabetes mellitus; and in patients who are unusually responsive to sympathomimetic amines. Large doses of intravenous albuterol have been reported to aggravate pre-existing diabetes mellitus and ketoacidosis Additionally, β-agonists may cause a decrease in serum potassium in some patients, possibly through intracellular shunting The decrease is usually transient, not requiring supplementation

2 Effects Seen with Anticholinergic Drugs. Due to the presence of ipratropium bromide in DuoNeb, it should be used with caution in patients with narrow-angle glaucoma, prostatic hypertrophy, or bladder-neck obstruction

3. Use in Hepatic or Renal Diseases: DuoNeb has not been studied in patients with hepatic or renal insufficiency It should be used with caution in these patient populations

Information for Patients

The action of DuoNeb should last up to 5 hours DuoNeb should not be used more frequently than recommended. Patients should be instructed not to increase the dose or frequency of DuoNeb without consulting their healthcare provider. If symptoms worsen, patients should be instructed to seek medical consultation

Patients must avoid exposing their eyes to this product as temporary papillary dilation, blurred vision, eye pain, or precipitation or worsening of narrow-angle glaucoma may occur, and therefore proper nebulizer technique should be assured, particularly if a mask is used

If a patient becomes pregnant or begins nursing while on DuoNeb, they should contact their healthcare provider about use of DuoNeb.

See the illustrated Patient's Instruction for Use in the product package insert

Drug Interactions

Anticholinergic agents: Although ipratropium bromide is minimally absorbed into the systemic circulation, there is some potential for an additive interaction with concomitantly used anticholinergic medications. Caution is, therefore, advised in the co-administration of DuoNeb with other drugs having anticholinergic properties

β-adrenergic agents. Caution is advised in the co-administration of DuoNeb and other sympathomimetic agents due to the increased risk of adverse cardiovascular effects

β-receptor blocking agents: These agents and albuterol sulfate inhibit the effect of each other β-receptor blocking agents should be used with caution in patients with hyperreactive airways, and if used, relatively selective β_1 selective agents are recommended

Diuretics: The electrocardiogram (ECG) changes and/or hypokalemia that may result from the administration of non-potassium sparing diuretics (such as loop or thiazide diuretics) can be acutely worsened by β-agonists, especially when the recommended dose of the β-agonist is exceeded Although the clinical significance of these effects is not known, caution is advised in the co-administration of β-agonist-containing drugs, such as DuoNeb, with non-potassium sparing diuretics

Monoamine oxidase inhibitors or tricyclic antidepressants DuoNeb should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, or within 2 weeks of discontinuation of such agents because the action of albuterol sulfate on the cardiovascular system may be potentiated

Carcinogenesis, Mutagenesis, Impairment of Fertility

Albuterol Sulfate: In a 2-year study in Sprague-Dawley rats, albuterol sulfate caused a significant dose-related increase in the incidence of benign leiomyomas of the mesovarium at and above dietary doses of 2 mg/kg (approximately equal to the maximum recommended daily inhalation dose for adults on a mg/m^2 basis). In another study, this effect was blocked by the coadministration of propranolol, a non-selective beta-adrenergic antagonist

In an 18-month study in CD-1 mice, albuterol sulfate showed no evidence of tumorigenicity at dietary doses up to 500 mg/kg (approximately 140 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis). In a 22-month study in Golden hamsters, albuterol sulfate showed no evidence of tumorigenicity at dietary doses up to 50 mg/kg (approximately 20 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis).

Albuterol sulfate was not mutagenic in the Ames test or a mutation test in yeast Albuterol sulfate was not clastogenic in a human peripheral lymphocyte assay or in an AH1 strain mouse micronucleous assay

Reproduction studies in rats demonstrated no evidence of impaired fertility at oral doses of albuterol sulfate up to 50 mg/kg (approximately 25 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis)

Ipratropium bromide: In 2-year studies in Sprague-Dawley rats and CD-1 mice, ipratropium bromide showed no evidence of tumorigenicity at oral doses up to 6 mg/kg (approximately 15 times and 8 times the maximum recommended daily inhalation dose for adults in rats and mice respectively, on a mg/m^2 basis)

Ipratropium bromide was not mutagenic in the Ames test and mouse dominant lethal test Ipratropium bromide was not clastogenic in a mouse micronucleous assay

A reproduction study in rats demonstrated decreased conception and increased resorptions when ipratropium bromide was administered orally at a dose of 90 mg/kg (approximately 240 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis). These effects were not seen with a dose of 50 mg/kg (approximately 140 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis).

Pregnancy

TERATOGENIC EFFECTS Pregnancy Category C

Albuterol sulfate: *Pregnancy Category C.* Albuterol sulfate has been shown to be teratogenic in mice A study in CD-1 mice given albuterol sulfate subcutaneously showed cleft palate formation in 5 of 111 (4.5%) fetuses at 0.25 mg/kg (less than the maximum recommended daily inhalation dose for adults on a mg/m^2 basis) and in 10 of 108 (9.3%) fetuses at 2.5 mg/kg (approximately equal to the maximum recommended daily inhalation dose for adults on a mg/m^2 basis). The drug did not induce cleft palate formation when administered subcutaneously at a dose of 0.025 mg/kg (less than the maximum recommended daily inhalation dose for adults on a mg/m^2 basis) Cleft palate formation also occurred in 22 of 72 (30.5%) fetuses from females treated subcutaneously with 2.5 mg/kg isoproterenol (positive control).

A reproduction study in Stride rabbits revealed cranioschisis in 7 of 19 (37%) fetuses when albuterol was administered orally at a dose of 50 mg/kg (approximately 55 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis).

A study in which pregnant rats were dosed with radiolabeled albuterol sulfate demonstrated that drug-related material is transferred from the maternal circulation to the fetus.

During worldwide marketing experience, various congenital anomalies, including cleft palate and limb defects, have been reported in the offspring of patients being treated with albuterol. Some of the mothers were taking multiple medications during their pregnancies Because no consistent pattern of defects can be discerned, a relationship between albuterol use and congenital anomalies has not been established

Ipratropium bromide: *Pregnancy Category B* Reproduction studies in CD-1 mice, Sprague-Dawley rats and New Zealand rabbits demonstrated no evidence of teratogenicity at oral doses up to 10, 100, and 125 mg/kg, respectively (approximately 15, 270, and 680 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis). Reproduction studies in rats and rabbits demonstrated no evidence of teratogenicity at inhalation doses up to 1.5 and 1.8 mg/kg, respectively (approximately 4 and 10 times the maximum recommended daily inhalation dose for adults on a mg/m^2 basis). There are no adequate and well-controlled studies of the use of DuoNeb, albuterol sulfate, or ipratropium bromide in pregnant women DuoNeb should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery

Oral albuterol sulfate has been shown to delay preterm labor in some reports Because of the potential of albuterol to interfere with uterine contractility, use of DuoNeb during labor should be restricted to those patients in whom the benefits clearly outweigh the risks

Nursing Mothers

It is not known whether the components of DuoNeb are excreted in human milk Although lipid-insoluble quaternary bases pass into breast milk, it is unlikely that ipratropium bromide would reach the infant to an important extent, especially when taken as a nebulized solution. Because of the potential for tumorigenicity shown for albuterol sulfate in some animals, a decision should be made whether to discontinue nursing or discontinue DuoNeb, taking into account the importance of the drug to the mother.

Pediatric Use

The safety and effectiveness of DuoNeb in patients below 18 years of age have not been established

Geriatric Use

Of the total number of subjects in clinical studies of DuoNeb, 62 percent were 65 and over, while 19 percent were 75 and over No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS

Adverse reaction information concerning DuoNeb was derived from the 12-week controlled clinical trial

ADVERSE EVENTS OCCURRING IN ≥ 1% OF ≥ 1 TREATMENT GROUP(S) AND WHERE THE COMBINATION TREATMENT SHOWED THE HIGHEST PERCENTAGE

Body System COSTART Term	Albuterol n (%)	Ipratropium n (%)	DuoNeb n (%)
NUMBER OF PATIENTS	761	754	765
N (%) Patients with AE	327 (43.0)	329 (43.6)	367 (48.0)
BODY AS A WHOLE			
Pain	8 (1.1)	4 (0.5)	10 (1.3)
Pain chest	11 (1.4)	14 (1.9)	20 (2.6)
DIGESTIVE			
Diarrhea	5 (0.7)	9 (1.2)	14 (1.8)
Dyspepsia	7 (0.9)	8 (1.1)	10 (1.3)
Nausea	7 (0.9)	6 (0.8)	11 (1.4)
MUSCULO-SKELETAL			
Cramps leg	8 (1.1)	6 (0.8)	11 (1.4)
RESPIRATORY			
Bronchitis	11 (1.4)	13 (1.7)	13 (1.7)
Lung Disease	36 (4.7)	34 (4.5)	49 (6.4)
Pharyngitis	27 (3.5)	27 (3.6)	34 (4.4)
Pneumonia	7 (0.9)	8 (1.1)	10 (1.3)
UROGENITAL			
Infection urinary tract	3 (0.4)	9 (1.2)	12 (1.6)

Additional adverse reactions reported in more than 1% of patients treated with DuoNeb included constipation and voice alterations

In the clinical trial, there was a 0.3% incidence of possible allergic-type reactions, including skin rash, pruritus, and urticaria

Additional information derived from the published literature on the use of albuterol sulfate and ipratropium bromide singly or in combination includes precipitation or worsening of narrow-angle glaucoma, acute eye pain, blurred vision, paradoxical bronchospasm, wheezing exacerbation of COPD symptoms, drowsiness, aching, flushing, upper respiratory tract infection, palpitations, taste perversion, elevated heart rate, sinusitis, back pain and sore throat.

DOSAGE AND ADMINISTRATION

The recommended dose of DuoNeb is one 3 mL vial administered 4 times per day via nebulization with up to 2 additional 3 mL doses allowed per day, if needed Safety and efficacy of additional doses or increased frequency of administration of DuoNeb beyond these guidelines has not been studied and the safety and efficacy of extra doses of albuterol sulfate or ipratropium bromide in addition to the recommended doses of DuoNeb have not been studied.

The use of DuoNeb can be continued as medically indicated to control recurring bouts of bronchospasm If a previously effective regimen fails to provide the usual relief, medical advice should be sought immediately, as this is often a sign of worsening COPD, which would require reassessment of therapy

A Pari-LC-Plus™ nebulizer (with face mask or mouthpiece) connected to a PRONEB™ compressor was used to deliver DuoNeb to each patient in one U.S. clinical study. The safety and efficacy of DuoNeb delivered by other nebulizers and compressors have not been established

DuoNeb should be administered via jet nebulizer connected to an air compressor with an adequate air flow, equipped with a mouthpiece or suitable face mask

HOW SUPPLIED

DuoNeb is supplied as a 3-mL sterile solution for nebulization in sterile low-density polyethylene unit-dose vials Cards of five vials are placed into a foil pouch Supplied in cartons as listed below.

NDC 49502-672-30	30 vials per carton
NDC 49502-672-60	60 vials per carton

Store between 2°C and 25°C (36°F and 77°F). Protect from light.

DEY

DEY, Napa, CA 94558

03-485-21(BRS) May 2001

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1 Gross N, Tashkin D, Miller R, et al. Inhalation by nebulization of albuterol-ipratropium combination (Dey combination) is superior to either agent alone in the treatment of chronic obstructive pulmonary disease. *Respiration.* 1998;65:354-362.

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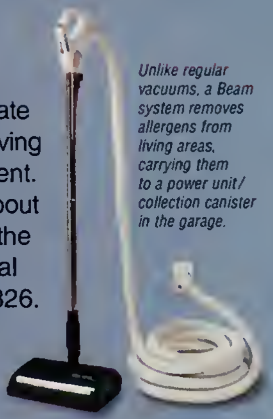

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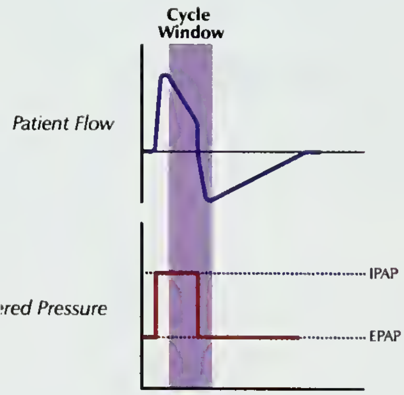
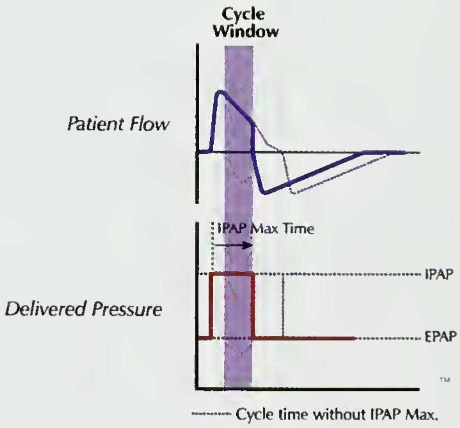
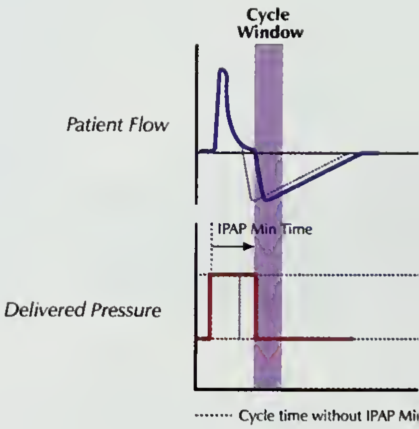


Normal Lungs
(Device cycles spontaneously within Cycle Window)



Obstructive Disease
(High Airway Resistance-Device cycles within Cycle Window at IPAP Max Time)



Restrictive Disease
(Device cycles within Cycle Window at IPAP Min Time)

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Editorials, Commentaries, and Reviews to Note

Treating Dyspnea in a Patient with Advanced Chronic Obstructive Pulmonary Disease—Runo JR, Ely EW. West J Med 2001 Sep;175(3):197-201.

Long-Acting Inhaled β_2-Agonist Therapy in Asthma—Kips JC, Pauwels RA. Am J Respir Crit Care Med 2001 Sep 15;164(6):923-932.

Weaning from Mechanical Ventilation: When Paediatric Intensive Care Medicine Profits from Adult Experience and Vice-Versa (editorial)—Brochard L. Intensive Care Med 2001 Oct;27(10):1564-1566.

COPD As a Muscle Disease (editorial)—Reid MB. Am J Respir Crit Care Med 2001 Oct 1;164(7):1101-1102.

Pro: The Increase in Asthma Can Be Ascribed to Cleanliness (editorial)—von Mutius E. Am J Respir Crit Care Med 2001 Oct 1;164(7):1106-1107; discussion 1108-1109.

Con: The Increase in Asthma Cannot Be Ascribed to Cleanliness (editorial)—Platts-Mills TA, Woodfolk JA, Sporik RB. Am J Respir Crit Care Med 2001 Oct 1;164(7):1107-1108; discussion 1108-1109.

Hold It! Correct Use of Inhalers in Children with Asthma—Abrolat ML, Nguyen LP, Saca LF. West J Med 2001 Nov;175(5):303-304.

Is Home Monitoring of Lung Function Worthwhile for Children with Asthma?—Sly PD, Flack F. West J Med 2001 Nov;175(5):344-345.

On the Use of Dry Powder Inhalers in Situations Perceived as Constrained—Borgstrom L. J Aerosol Med 2001 Fall;14(3):281-287.

Dose delivery from dry powder inhalers (DPIs) are dependent on the inhalation effort of the patient. Some patient groups, including asthmatic children, patients with acute asthma, and patients with advanced chronic obstructive pulmonary disease (COPD) are perceived as having problems in readily inhaling from a DPI in an efficient way: this opinion is based on alleged low inhalation flows. A review of the literature however shows that these groups can use a DPI in an efficient way and gain good clinical effect from its use. Particularly, it has been shown that children can generate a good peak inhalation flow through a DPI, albeit a lower inhaled volume. Similarly, patients with acute asthma can use a DPI in an efficient way, even reaching a better clinical effect with the DPI than with a pressurized metered dose inhaler with a spacer. Finally, it was shown that patients with severe COPD can generate the inhalation flows needed to generate an efficient drug aerosol from a DPI. Collectively, the discussed patient groups seem to perform as well as other subjects when it comes to their ability to generate an adequate inhalation flow through a DPI.

Effective Delivery of Particles with the Handihaler Dry Powder Inhalation System Over a Range of Chronic Obstructive Pulmonary Disease Severity—Chodosh S, Flanders JS, Kesten S, Serby CW, Hochrainer D, Witek TJ Jr. J Aerosol Med 2001 Fall;14(3):309-315.

The HandiHaler is a dry powder breath activated inhaler system developed for inhalation therapy for patients with airway disease. Its operation is based on the evacuation of powder from a pierced capsule. We sought to document the inspiratory flow rates attained by patients inspiring through the HandiHaler with various degrees of airflow limitation. Subjects with stable chronic obstructive pulmonary disease (COPD) were the study's population. An in vitro study of fine particle dose was conducted using an Andersen Cascade Impactor to assess medication delivery at low inspiratory flow rates. Subsequently, an in vivo study was conducted to determine inspiratory flow rates in patients with COPD as measured through a pneumotach with a custom coupler device with and without the HandiHaler. Patients were classified into three approximately equal groups of spirometric severity ranging from mild (46-65% predicted normal forced expiratory volume in 1 sec [FEV_1]), to moderate (28-45%) to severe (≤ 27%). The in vitro study indicated delivery of medication at flow rates as low as 20 L/min. Twenty-six men completed the in vivo study (age 66.9 ± 10.9 years, FEV_1 = 1.02 ± 0.45 L). The median peak inspiratory flow rates attained in the mild (n = 8), moderate (n = 10), and severe (n = 8) categories were 45, 45.6, and 35.4 L/min respectively. The minimum peak inspiratory flow rates in the three groups were 28.2, 21.6 and 20.4 L/min. The HandiHaler device effectively delivers particles to the lung over a wide range of airflow limitation in patients with COPD.

Breathing Patterns and Aerosol Delivery: Impact of Regular Human Patterns, and Sine and Square Waveforms on Rate of Delivery—Nikander K, Denyer J, Smith N, Wollmer P. J Aerosol Med 2001 Fall;14(3):327-333.

In vitro tests are commonly employed to assess nebulizer performance. Whether the square or sine waveforms employed during in vitro tests could alter the nebulizer performance compared to that observed when a patient breathes through the nebulizer is debatable. Accordingly, the aim of this in vitro study was to compare the rates of delivery from nebulizers

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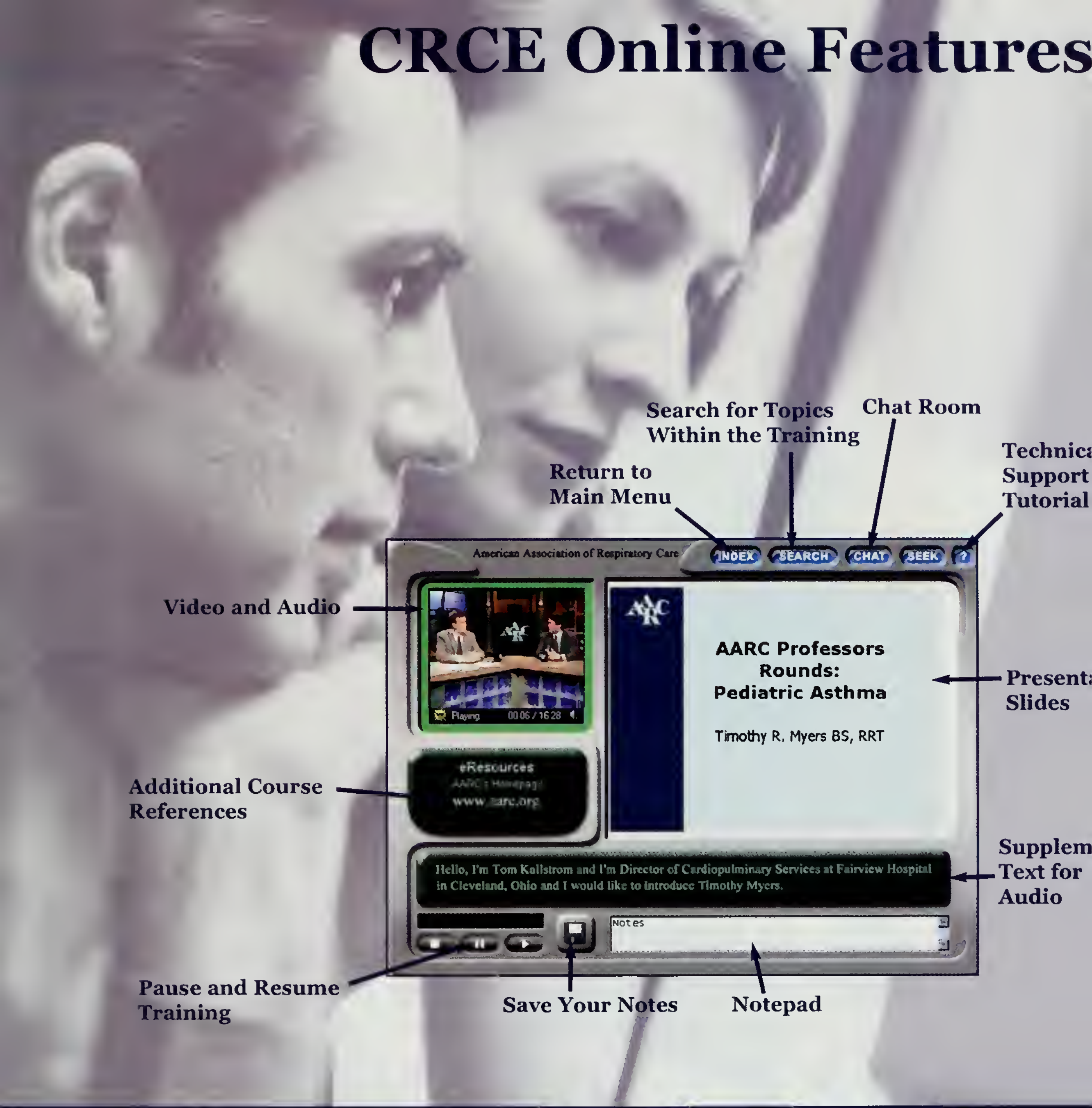

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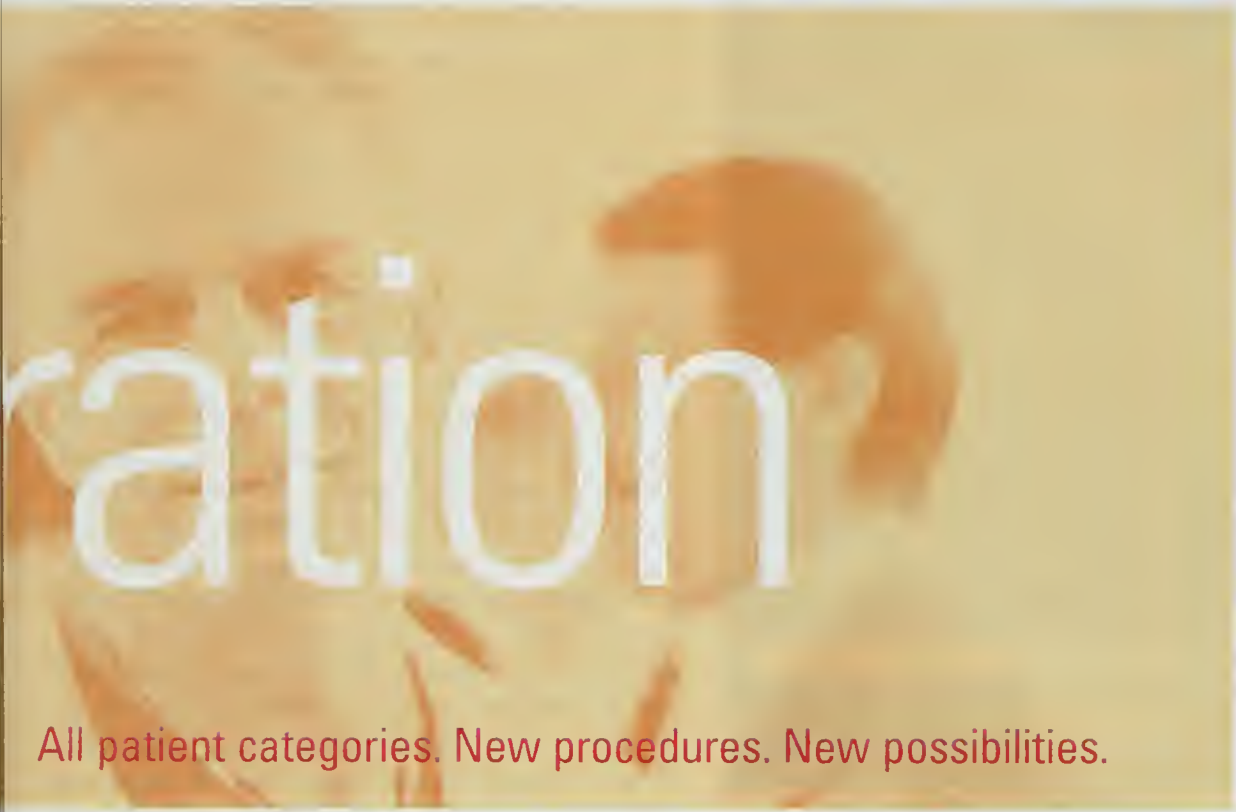
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with simulated human breathing patterns to those obtained with matching sine and square waveforms. Regular human breathing patterns with tidal volumes (V_T) of ~ 40, ~ 200, ~ 500, and ~ 800 mL were selected. Sine and square waveforms that matched the V_T, peak inspiratory flow rate (PIF), breathing frequency (f), and inspiratory duty cycle (t_i/t_{tot}) of the human breathing patterns were created with a breathing simulator. The rate of delivery of nebulized technetium-99m-labeled diethylenetriamine pentaacetic acid (^{99m}TC-DTPA) from two different jet nebulizer brands was determined. The rate of delivery was defined as the amount of the ^{99m}TC-DTPA deposited during 30 sec of nebulization on a filter placed between the nebulizer and the breathing simulator. The rate of delivery of ^{99m}TC-DTPA with the human breathing pattern was similar to that measured with the matching sine or square waveforms for either nebulizer. The configuration of the breath (PIF, V_T, f, t_i/t_{tot}) did, however, influence the rate of delivery. In conclusion, the shape of the waveform, in other words, one resulting from a human breathing pattern, or a matching sine or square waveform, did not influence the rate of ^{99m}TC-DTPA delivery from a nebulizer in vitro.

Effects of Inhaled Salbutamol in Exercising Non-Asthmatic Athletes—Goubault C, Perault MC, Leleu E, Bouquet S, Legros P, Vandel B, Denjean A. Thorax 2001 Sep;56(9):675-679.

BACKGROUND: β_2 agonists such as salbutamol are used, not only by asthmatic athletes to prevent exercise induced asthma, but also by non-asthmatic athletes as a potentially ergogenic agent. We have investigated whether inhaled salbutamol enhances endurance performance in non-asthmatic athletes. METHODS: A prospective double blind, randomised, three way crossover design was used to study the effects of 200 μg and 800 μg inhaled salbutamol versus a placebo in 12 trained triathletes. The treatments were compared in three identical cycle ergometer sessions at 85% of the predetermined maximal oxygen uptake. Lung function, endurance time, metabolic parameters (glucose, potassium, lactate, free fatty acid, and glycerol), and psychomotor performance were evaluated. RESULTS: Neither endurance time nor post-exercise bronchodilation were significantly different between the treatments. Metabolic parameters were affected by exercise but not by treatment. CONCLUSIONS: Inhaled salbutamol, even in a high dose, did not have a significant effect on endurance performance in non-asthmatic athletes, although the bronchodilating effect of the drug at the beginning of exercise may have improved respiratory adaptation. Our results do not preclude an ergogenic effect of β_2 agonists given by other routes or for a longer period.

Airway Function at One Year: Association with Premorbid Airway Function, Wheezing, and Maternal Smoking—Dezateux C, Stocks J, Wade AM, Dundas I, Fletcher ME. Thorax 2001 Sep;56(9):680-686.

BACKGROUND: Impaired growth and development of the respiratory system during fetal and early postnatal life may have important implications for lung development and later lung health. The aim of this study was to examine the association of diminished premorbid airway function, prior wheezing, and maternal smoking with airway function at 1 year of age. METHODS: Respiratory function was measured at the end of the first year in 100 of 108 healthy term infants (93%) in whom similar measurements had been undertaken prior to any respiratory illness at 8 weeks. Physician diagnosed wheezing episodes were identified retrospectively from medical records. RESULTS: At 1 year specific airway conductance during end expiration (sGawEE; /s/kPa) was significantly diminished in those infants with prior wheezing (95% CI wheeze/no wheeze -0.76 to -0.14), mothers who smoked (95% CI smoke/no smoke -0.81 to -0.27), a family history of asthma (95% CI family history/no family history -0.62 to 0.00), or diminished premorbid sGawEE (95% CI -0.13 to -0.43/s/kPa per unit reduction sGawEE at 8 weeks). In a multivariate model only maternal smoking and diminished premorbid sGawEE were independently associated with diminished sGawEE at 1 year. CONCLUSIONS: Diminished airway function at the end of the first year appears to be mediated by impaired airway development during early life as well as by exposure to maternal smoking. These findings are consistent with the hypothesis that, at a population level, diminished premorbid airway function provides the link between wheezing lower respiratory illness and diminished airway function at 1 year. Maternal smoking remains an important and avoidable cause of impaired airway development and function in infancy.

Changing Patterns of Hospital Admission for Asthma, 1981-97—Morrison DS, McLoone P. Thorax 2001 Sep;56(9):687-690.

BACKGROUND: Hospital admission rates for asthma have stopped rising in several countries. The aim of this study was to use linked hospital admission data to explore recent trends in asthma admissions in Scotland. METHODS: Linked Scottish Morbidity Records (SMR1) for asthma (ICD-9 493 and ICD-10 J45-6) from 1981 to 1997 were used to describe rates of first admissions and readmissions by age and sex. As a measure of resource use, annual trends in bed days used were also explored by age and sex. RESULTS: There were 160 039 hospital admissions for asthma by 82 421 individuals in Scotland during the study period. The overall hospital admission rate increased by 122% (from 106.7 to 236.7 per 100 000 population) but this varied by sex, age, and admission type. First admissions rose by 70% from 73.2 per 100 000 in 1986 to 124.8 per 100 000 in 1997 while readmissions fell. Children (<15 years) experienced a decline in overall admissions after 1992 due to falls in both new admissions and readmissions. By 1997 the ratio of female to male admissions was 0.57 in children, but 1.50 above 14 years of age. Mean lengths of stay fell from 10.7 days to 3.7 days between 1981 and 1997 and bed days used showed little change except for a decline after 1992 in children. CONCLUSIONS: After a period of increasing hospitalisation for asthma in Scotland, rates of admission among children have begun to fall but among adults admissions continue to rise.

Reference Values of Interrupter Respiratory Resistance in Healthy Preschool White Children—Lombardi E, Sly PD, Concutelli G, Novembre E, Veneruso G, Frongia G, et al. Thorax 2001 Sep;56(9):691-695.

BACKGROUND: Interrupter respiratory resistance (Rint) is reported to be useful in evaluating lung function in poorly collaborating patients. However, no reference values are available from large samples of preschool children using the standard interrupter method. The aim of this study was to define reference Rint values in a population of healthy preschool children. METHODS: Rint was assessed without supporting the cheeks in children with no history of wheeze from six kindergartens. To evaluate the effects of upper airway compliance on Rint in healthy children, an additional group of preschool children with either no history of wheeze or no respiratory symptoms at the time of testing underwent Rint measurements in our lung function laboratory with and without supporting the cheeks. Short term (about 1 minute apart) and long term (mean 2.5 months apart) repeatability of Rint measurements (2 SDs of the mean paired difference between measurements) was also assessed in children referred for cough or wheeze. RESULTS: A total of 284 healthy white children (age range 3.0-6.4 years) were evaluated. Mean inspiratory and expiratory Rint (RintI and RintE) did not differ significantly in boys and girls. Age, height, and weight showed a significant inverse correlation with both RintI and RintE in the univariate analysis with linear regression. Multiple regression with age, height, and weight as the independent variables showed that all three variables were significantly and independently correlated with RintI, whereas only height was significantly and independently correlated with RintE. Supporting the cheeks had no significant effect on RintI (n=29, median 0.673 v 0.660 kPa/L t s, p=0.098) or RintE (n=39, median 0.702 v 0.713 kPa/L t s, p=0.126). Short term repeatability was 0.202 kPa/ L · s for RintI (n=50) and 0.242 kPa/ L · s for RintE (n=69). Long term repeatability was 0.208 kPa/ L · s for RintE (n=26). CONCLUSIONS: We have reported reference Rint values in preschool white children and have demonstrated the usefulness of this technique in assessing lung function in this age group.

Non-Invasive Ventilation in Acute Exacerbations of Chronic Obstructive Pulmonary Disease: Long Term Survival and Predictors of In-Hospital Outcome—Plant PK, Owen JL, Elliott MW. Thorax 2001 Sep;56(9):708-712.

BACKGROUND: Non-invasive ventilation (NIV) reduces the need for intubation and the mortality associated with an exacerbation of chronic obstructive pulmonary disease (COPD). This study aimed to identify factors that could be used to stratify patients according to their risk of requiring invasive mechanical ventilation. The second aim was to determine the long term survival of patients treated with and without NIV. METHODS: In this prospective multicentre randomised controlled trial 118 patients were allocated to standard treatment and 118 to NIV between November 1996 and September 1998. Arterial blood gas tensions and respiratory rate were recorded at enrolment and after 1 and 4 hours. Prognostic factors were identified using logistic regression analysis. All patients were followed until death or 1 January 1999. RESULTS: At enrolment the H^+ concentration (OR 1.22 per nmol/L, 95% CI 1.09 to 1.37, $p < 0.01$) and $P_{a}co_2$ (OR 1.14 per kPa, 95% CI 1.14 to 1.81, $p<0.01$) were associated with treatment failure. Allocation to NIV was protective (OR 0.39, 95% CI 0.19 to 0.80). After 4 hours of treatment improvement in acidosis (OR

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0.89 per nmol/L, 95% CI 0.82 to 0.97, p<0.01) and fall in respiratory rate (OR 0.92 per breaths/min, 95% CI 0.84 to 0.99, p=0.04) were associated with success. Median length of survival was 16.8 months in those treated with NIV and 13.4 months in those receiving standard treatment (p=0.12). The trend in improved survival was attributable to prevention of death during the index admission. CONCLUSION: Initial pH and hypercapnia can be used to stratify groups of patients according to their risk of needing intubation. NIV reduces this risk and progress should be monitored using change in respiratory rate and pH. The long term survival after NIV is sufficiently good to render treatment appropriate.

Systematic Review of Clinical Effectiveness of Pressurised Metered Dose Inhalers Versus Other Hand Held Inhaler Devices for Delivering Corticosteroids in Asthma—Brocklebank D, Wright J, Cates C. BMJ 2001 Oct 20;323(7318):896-900.

OBJECTIVE: To determine the clinical effectiveness of pressurised metered dose inhalers (with or without spacer) compared with other hand held inhaler devices for the delivery of corticosteroids in stable asthma. DESIGN: Systematic review of randomised controlled trials. DATA SOURCES: Cochrane Airways Group trials database (Medline, Embase, Cochrane controlled clinical trials register, and hand searching of 18 relevant journals), pharmaceutical companies, and bibliographies of included trials. Trials: All trials in children or adults with stable asthma that compared a pressurised metered dose inhaler with any other hand held inhaler device delivering the same inhaled corticosteroid. RESULTS: 24 randomised controlled trials were included. Significant differences were found for forced expiratory volume in one second, morning peak expiratory flow rate, and use of drugs for additional relief with dry powder inhalers. However, either these were within clinically equivalent limits or the differences were not apparent once baseline characteristics had been taken into account. No significant differences were found between pressurised metered dose inhalers and any other hand held inhaler device for the following outcomes: lung function, symptoms, bronchial hyper-reactivity, systemic bioavailability, and use of additional relief bronchodilators. CONCLUSIONS: No evidence was found that alternative inhaler devices (dry powder inhalers, breath actuated pressurised metered dose inhalers, or hydrofluoroalkane pressurised metered dose inhalers) are more effective than the pressurised metered dose inhalers for delivery of inhaled corticosteroids. Pressurised metered dose inhalers remain the most cost effective first line delivery devices.

Systematic Review of Clinical Effectiveness of Pressorised Metered Dose Inhalers Versus Other Hand Held Inhaler Devices for Delivering β_2 Agonists Bronchodilators in Asthma—Ram FS, Wright J, Brocklebank D, White JE. BMJ 2001 Oct 20;323(7318):901-905.

OBJECTIVES: To determine the clinical effectiveness of pressurised metered dose inhalers compared with other hand held inhaler devices for delivering short acting β_2 agonists in stable asthma. DESIGN: Systematic review of randomised controlled trials. DATA SOURCES: Cochrane Airways Group specialised trials database (which includes hand searching of 20 relevant journals), Medline, Embase, Cochrane controlled clinical trials register, pharmaceutical companies, and bibliographies of included trials. TRIALS: All trials in children or adults with stable asthma that compared the pressurised metered dose inhaler (with or without a spacer device) against any other hand held inhaler device containing the same β_2 agonist. Results: 84 randomised controlled trials were included. No differences were found between the pressurised metered dose inhaler and any other hand held inhaler device for lung function, blood pressure, symptoms, bronchial hyperreactivity, systemic bioavailability, inhaled steroid requirement, serum potassium concentration, and use of additional relief bronchodilators. In adults, pulse rate was lower in those using the pressurised metered dose inhaler compared with those using Turbohaler (standardised mean difference 0.44, 95% confidence interval 0.05 to 0.84); patients preferred the pressurised metered dose inhaler to the Rotahaler (relative risk 0.53, 95% confidence interval 0.36 to 0.78); hydrofluoroalkane pressurised metered dose inhalers reduced the requirement for rescue short course oral steroids (relative risk 0.67, 0.49 to 0.91). CONCLUSIONS: No evidence was found to show that alternative inhaler devices are more effective than standard pressurised metered dose inhalers for delivering acting β_2 agonist bronchodilators in asthma. Pressurised metered dose inhalers remain the most cost effective delivery devices.

Alternative Methods for Assessing Bronchodilator Reversibility in Chronic Obstructive Pulmonary Disease—Hadcroft J, Calverley PM. Thorax 2001 Sep;56(9):713-720.

BACKGROUND: Bronchodilator reversibility testing is recommended in all patients with chronic obstructive pulmonary disease (COPD) but does not predict improvements in breathlessness or exercise performance. Two alternative ways of assessing lung mechanics—measurement of end expiratory lung volume (EELV) using the inspiratory capacity manoeuvre and application of negative expiratory pressure (NEP) during tidal breathing to detect tidal airflow limitation—do relate to the degree of breathlessness in COPD. Their usefulness as end points in bronchodilator reversibility testing has not been examined. METHODS: We studied 20 patients with clinically stable COPD (mean age 69.9 (1.5) years, 15 men, forced expiratory volume in one second (FEV$_1$) 29.5 (1.6)% predicted) with tidal flow limitation as assessed by their maximum flow-volume loop. Spirometric parameters, slow vital capacity (SVC), inspiratory capacity (IC), and NEP were measured seated, before and after nebulised saline, and at intervals after 5 mg nebulised salbutamol and 500 microg nebulised ipratropium bromide. The patients attended twice and the treatment order was randomised. RESULTS: Mean FEV$_1$, FVC, SVC, and IC were unchanged after saline but the degree of tidal flow limitation varied. FEV$_1$ improved significantly after salbutamol and ipratropium (0.11 (0.02) L and 0.09 (0.02) L, respectively) as did the other lung volumes with further significant increases after the combination. Tidal volume and mean expiratory flow increased significantly after all bronchodilators but breathlessness fell significantly only after the combination treatment. The initial NEP score was unrelated to subsequent changes in lung volume. CONCLUSIONS: NEP is not an appropriate measurement of acute bronchodilator responsiveness. Changes in IC were significantly larger than those in FEV$_1$ and may be more easily detected. However, our data showed no evidence for separation of "reversible" and "irreversible" groups whatever outcome measure was adopted.

Continuous Positive Airway Pressure for Sleep Apnoea/Hypopnoea Syndrome: Usefulness of a 2 Week Trial to Identify Factors Associated with Long Term Use—Popescu G, Latham M, Allgar V, Elliott MW. Thorax 2001 Sep;56(9):727-733.

BACKGROUND: The sleep apnoea/hypopnoea syndrome (SAHS) is common and treatment with continuous positive airway pressure (CPAP) is effective. However, not all patients can cope with the demands of using mask positive pressure. Compliance can be improved with an intensive educational programme and patient support, but this is not practical in most centres given the large numbers of patients coming forward for treatment. Several studies have evaluated correlations between various parameters at diagnosis in order to anticipate patients' behaviour and to avoid the social and health implications of undertreated SAHS. We have evaluated the use of additional data derived during a 2 week home CPAP trial to identify factors associated with longer term use of CPAP and compliance. METHODS: Following a diagnostic study, 209 patients were offered a CPAP machine for a 2 week home trial. After completing the trial, patients were reassessed and scored their overall satisfaction with CPAP treatment on a five point scale ranging from "much worse" to "much better" and an Epworth score relating to the loan period. Machine run time was recorded from the integral clock. These data were added to those available at diagnosis to construct models indicative of continuing CPAP and average nightly use at 1 year. RESULTS: 209 patients were offered the 2 week loan at least a year before June 1999 (90.9% men, mean (SD) age 51.0 (10.6) years, body mass index (BMI) 34.6 (7.7) kg/m^2, Epworth score 15 (IQR 11-18), apnoea/hypopnoea index (AHI) 38.1 (22.9) events/h). 153 patients (73.2%) opted to continue CPAP and 56 declined. One year later data were available for 187 patients; 128 (68.5% on an intention to treat analysis) continued to use the machine with a mean use of 5.0 (2.4) hours/night. A logistic regression model indicated that mean CPAP use during the loan period and the overall satisfaction score accurately defined continuing CPAP and "satisfactory" CPAP use at 1 year. For patients with low machine use and no symptomatic improvement during the loan period, the addition of baseline AHI, baseline Epworth score, and the Epworth score at the end of the loan to the equation identifying factors associated with "satisfactory" CPAP use (mean >2 hours/night) improved the value of the model. CONCLUSION: Data derived from a 2 week CPAP trial are useful in identifying patients who will comply with CPAP treatment to 1 year. It can be used to identify patients with significant symptomatic disease who will struggle with CPAP and may benefit from additional education and support. High mean hourly use and a high degree of overall satisfaction during the loan period identified patients likely to use CPAP and be compliant with it at 1 year.

A Comparison of the Lung Deposition of Budesonide from Easyhaler, Turbuhaler and pMDI Plus Spacer in Asthmatic Patients—Hirst PH, Bacon RE, Pitcairn GR, Silvasti M, Newman SP. Respir Med 2001 Sep;95(9):720-727.

Inhaled corticosteroids in pressurized metered does inhalers (pMDIs) are often delivered via a large volume spacer device, but these are bulky and inconvenient. Dry powder inhalers (DPIs) provide a highly portable and convenient propellant-free alternative to pMDIs for asthma maintenance therapy However, each DPI could have unique in vivo delivery characteristics. In order to quantify the total and regional lung deposition of budesonide (200 μg) from (a) Easyhaler, (b) Turbuhaler and (c) pMDI plus Nebuhaler 750 mL spacer, a three-way randomized cross-over study was carried out in 12 mild to moderate asthmatic patients. Deposition was quantified by the imaging technique of gamma scintigraphy Optimal inhalation techniques were used throughout. Mean (SD) whole lung deposition (% metered dose) was similar for Easyhaler [18.5 (7.8) %] and Turbuhaler [21.8 (8.2) %], but was significantly higher for pMDI plus Nebuhaler [44.1 (10.0) %, $p < 0.01$]. The regional distribution patterns in the lungs were predominantly central for all three devices. Nebuhaler reduced oropharyngeal deposition significantly compared with the two DPIs. Easyhaler showed comparable deposition to Turbuhaler and hence drugs delivered by Easyhaler would be expected to have a similar clinical effect to those delivered by Turbuhaler in asthma maintenance therapy.

Screening of Obstructive Sleep Apnoea: Heart Rate Spectral Analysis of Nocturnal Pulse Oximetric Recording—Zamarron C, Romero PV, Gude F, Amaro A, Rodriguez JR. Respir Med 2001 Sep;95(9):759-765.

Using heart rate spectral analysis of nocturnal pulse oximetry, we prospectively evaluated the utility of this methodology in patients clinically suspected of having obstructive sleep apnoea (OSA). A hundred and ninety-seven outpatients referred with symptoms compatible with the diagnosis of OSA were studied. All participants had nocturnal pulse oximetry performed simultaneously with conventional polysomnography. Power density of heart rate obtained by nocturnal pulse oximetry was analysed using fast Fourier transformation of a Hamming-windowed signal. Recording test results were classified as abnormal (suspicion of OSA) in the presence of a peak in the periodogram between period

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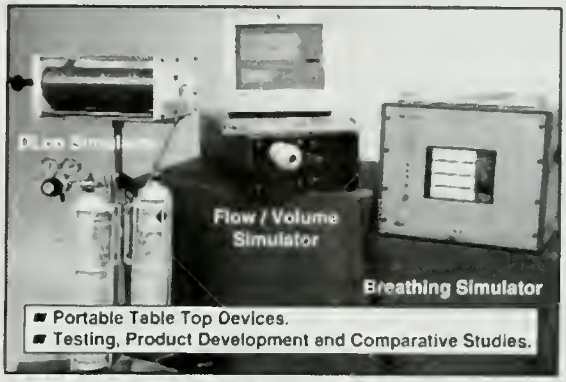

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boundaries 30-70 sec. A normal test result was defined as the absence of the 30-70 sec peak in the periodogram. The total area of the periodogram (S_{TOT}), the area enclosed in the periodogram between the period boundaries 30-70 sec (S_{30-70}), the area enclosed in the period boundaries 30-70 sec with respect to the total area of the periodogram (S) and the peak amplitude 30-70 sec (PA) were measured. The presence of a peak in the periodogram has a sensitivity of 81.3%, a specificity of 91.5% a positive predictive value of 89.1% and a negative predictive value of 85.1% for OSA diagnosis. The OSA patients were found to have higher values of S_{TOT}, S_{30-70}, S and PA than the non OSA patients. Receiver operating characteristics (ROC) curve was constructed at different thresholds of S_{TOT}, S_{30-70} S and PA. For a PA threshold of 10(%)2, heart rate spectra analysis sensitivity for OSA was 58% and specificity was 92%. Furthermore, the positive and negative predictive values for diagnosis of OSA were 87 and 72% respectively. Apnoea hypopnea index (AHI) correlated significantly with S_{TOT} ($r=0.44$; $p<0.001$), S_{30-70} ($r=0.59$: $p<0.001$), S ($r=0.58$; $p<0.001$) and PA ($r=0.58$; $p<0.001$). According to our results, heart rate spectral analys s obtained by nocturnal pulse oximetry and identification of peak in the periodogram between period boundaries 30-70 sec could be useful as a diagnostic technique for OSA patients.

Impact of a Pediatric Asthma Clinical Pathway on Hospital Cost and Length of Stay—Wazeka A, Valacer DJ, Cooper M, Caplan DW, DiMaio M. Pediatr Pulmonol 2001 Sep;32(3):211-216.

This study sought to determine if a clinical pathway developed and executed by specialists in pediatric asthma would reduce hospital costs and length of stay (LOS). The study design was a retrospective, nonrandomized, controlled trial. Subjects were children aged 2-18 years (N = 1,004) with a history of recurrent wheezing, hospitalized with a diagnosis of acute asthma exacerbation between 1995-1998 at the New York Hospital-Weill Cornell Medical Center and treated via the pathway, as well as a control group of 206 children ages 2-18 hospitalized for acute asthma exacerbation in 1994, the year prior to pathway implementation. Patients were treated via the pathway under the supervision of an asthma specialist. The pathway provided guidelines for: 1) frequency of patient assessment; 2) bronchodilator usage; 3) corticosteroid use; 4) laboratory evaluation; 5) vital signs, oxygen saturation, and peak flow measurements; 6) chest x-rays; 7) social work intervention; and 8) discharge planning. The main outcome measures were hospital length of stay, cost per hospitalization, nursing, medication, laboratory and radiology costs, and relapse rate. Total charges for admission and average LOS for 1995-1998 were calculated, and compared with 1994, the year preceding implementation of the pathway. LOS decreased from 4.2 days to 2.7 days ($p < 0.0001$). The annual total charges for pediatric asthma admissions decreased from 2 million dollars to 1.4 million dollars ($p < 0.005$). Nursing and laboratory costs showed a statistically significant decrease. Follow-up study at 8 months showed a readmission rate of 0.02%. The implementation of a pediatric asthma clinical pathway, directed by specialists, resulted in significantly decreased length of stay and overall cost, without an increased rate of readmission.

Lung Function Testing in Infants with Cystic Fibrosis: Lessons from the Past and Future Directions—Gappa M, Ranganathan SC, Stocks J. Pediatr Pulmonol 2001 Sep;32(3):228-245.

Despite the increasing awareness of the need to identify early pulmonary changes in cystic fibrosis (CF) noninvasively, the role of lung function testing in infancy and early childhood remains less clear than in older children with CF. The aim of this review is to summarize available data, discuss the information gained from these publications, and put this information into perspective with more recent developments of lung function testing in both infants and older children with CF. While some of the available data have been the foundation of the current level of understanding of respiratory physiology in CF, interpretation of other data has been hampered by differences between centers with regard to the methods and equipment used, patient selection, small number of subjects, and lack of appropriate reference data. A structured multicenter approach based on recently published recommendations for the measurement of lung function in infancy, together with pursuit of recent developments such as assessment of raised lung volume flow volume curves and ventilation inhomogeneity may help to more effectively utilize lung function tests in infants in the future.

Postoperative Complications in Patients with Obstructive Sleep Apnea Syndrome Undergoing Hip or Knee Replacement: A Case-Control Study—Gupta RM, Parvizi J, Hanssen AD, Gay PC. Mayo Clin Proc 2001 Sep;76(9):897-905.

OBJECTIVE: To identify and assess the impact of postoperative complications in patients with unrecognized or known obstructive sleep apnea syndrome (OSAS) undergoing hip replacement or knee replacement compared with control patients undergoing similar operations. Although OSAS is a risk factor for perioperative morbidity, data quantifying the magnitude of the problem in patients undergoing non-upper airway operations are limited. PATIENTS AND METHODS: This retrospective, case-control study from a single academic medical institution included patients diagnosed as having OSAS between January 1995 and December 1998 and undergoing hip or knee replacement within 3 years before or anytime after their OSAS diagnosis. Patients with OSAS were subcategorized as having the diagnosis either before or after the surgery and also, regardless of time of diagnosis, by whether they were using continuous positive airway pressure (CPAP) prior to hospitalization. Matched controls were patients without OSAS undergoing the same operation. Interventions were defined specifically as administration of a particular treatment in the context of each complication, eg, supplemental oxygen, implementation of additional monitoring such as oximetry for hypoxemia, or transfer to the intensive care unit (ICU) for cardiac ischemia concerns. Postoperative complications were assessed for all patients in the different categories and included respiratory events such as hypoxemia, acute hypercapnia, and episodes of delirium. Serious complications were noted separately, including unplanned ICU days, reintubations, and cardiac events. The length of hospital stay was also tabulated. RESULTS: There were 101 patients with the diagnosis of OSAS in this study and 101 matched controls. Thirty-six patients had their joint replacement before OSAS was diagnosed, and 65 had surgery after OSAS was diagnosed. Of the latter 65 patients, only 33 were using CPAP at home preoperatively. Complications were noted in 39 patients (39%) in the OSAS group and 18 patients (18%) in the control group ($P=0.001$). Serious complications occurred in 24 patients (24%) in the OSAS group compared with 9 patients (9%) in the control group ($P=0.004$). Hospital stay was significantly longer for the OSAS patients at a mean ± SD of 6.8 ± 2.8 days compared with 5.1 ± 4.1 days for the control patients ($p<0.007$). CONCLUSION: Adverse postoperative outcomes occurred at a higher rate in patients with a diagnosis of OSAS undergoing hip or knee replacement compared with a group of matched control patients.

Diagnosis and Treatment of Allergic Bronchopulmonary Aspergillosis—Vlahakis NE, Aksamit TR. Mayo Clin Proc 2001 Sep;76(9):930-938.

Allergic bronchopulmonary aspergillosis (ABPA) is an underdiagnosed pulmonary disorder in asthmatic patients and patients with cystic fibrosis. Its clinical and diagnostic manifestations arise from an allergic response to multiple antigens expressed by fungi, most commonly *Aspergillus fumigatus*, colonizing the bronchial mucus. The clinical course is one of recurrent exacerbations characterized by chest infiltrates evident on chest x-ray films and associated with cough, wheeze, and sputum production that usually respond to oral corticosteroid treatment. Specific immunologic and radiologic markers of disease include elevation of the total serum IgE levels, presence of aspergillus IgE antibodies, and the occurrence of central bronchiectasis. Long-term treatment with corticosteroids is often required for effective management. The adverse effects of chronic corticosteroid use have led to attempts at treatment with antifungal agents such as itraconazole. Itraconazole has been reported anecdotally to be effective, and evidence for its effectiveness in randomized trials is still accruing. Consideration should be given to its use as a corticosteroid-sparing agent or for treatment of patients in whom corticosteroid response is poor. The natural history and prognosis of ABPA are not well characterized but may be complicated by progression to bronchiectasis and pulmonary fibrosis. If ABPA is diagnosed and treated before the development of bronchiectasis and fibrosis, these complications may be prevented.

Relationship Between the Duration of the Preoperative Smoke-Free Period and the Incidence of Postoperative Pulmonary Complications After Pulmonary Surgery—Nakagawa M, Tanaka H, Tsukuma H, Kishi Y. Chest 2001 Sep;120(3):705-710.

STUDY OBJECTIVE: To examine the relationship between the duration of the preoperative smoke-free period and the development of postoperative pulmonary complications (PPCs) in patients who underwent pulmonary surgery, and the optimal timing of quitting smoking. DESIGN: Retrospective cohort study. SETTING: Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan. PATIENTS: Two hundred eighty-eight consecutive patients who underwent pulmonary surgery between January 1997 and December 1998. Measurements and results: We collected information on the preoperative characteristics, intraoperative conditions, and occurrence of PPCs by reviewing the medical records. Study subjects were classified into four groups based on their smoking status. A current smoker was defined as one who smoked within 2 weeks prior to the operation. Recent smokers and ex-smokers were defined as those whose duration of abstinence from smoking was 2 to 4 weeks and > 4 weeks prior to the operation, respectively. A never-smoker was defined as one who had never smoked. The incidence of PPCs among the current smokers and recent smokers was 43.6% and 53.8%, respectively, and each was higher than that in the never-smokers (23.9%; $p < 0.05$). The moving average of the incidence of PPCs gradually decreased in patients whose smoke-free period was 5 to 8 weeks or longer. After controlling for sex, age, results of pulmonary function tests, and duration of surgery, the odds ratios for PPCs developing in current smokers, recent smokers, and ex-smokers in comparison with never-smokers were 2.09 (95% confidence interval [CI], 0.83 to 5.25), 2.44 (95% CI, 0.67 to 8.89), and 1.03 (95% CI, 0.47 to 2.26), respectively. CONCLUSIONS: These findings indicate that preoperative smoking abstinence of at least 4 weeks is necessary for patients who undergo pulmonary surgery, to reduce the incidence of PPCs.

Environmental Tobacco Smoke Exposure During Childhood Is Associated with Increased Prevalence of Asthma in Adults—Larsson ML, Frisk M, Hallstrom J, Kiviloog J, Lundback B. Chest 2001 Sep;120(3):711-717.

OBJECTIVE: To examine if exposure to environmental tobacco smoke (ETS) during childhood has an impact on asthma prevalence in adults, and to identify the amount of nuisance from ETS and other lower airway irritants (LAWIs) in a city population. DESIGN: A postal survey. SETTING: The municipality of Orebro, Sweden. PARTICIPANTS: A total of 8,008 randomly selected inhabitants aged 15 to 69 years. MEASUREMENTS: Exposures, airway symptoms, and respiratory history were assessed using a questionnaire. RESULTS: The response rate was 84%. In never-smokers with childhood ETS exposure, the prevalence of physician-diagnosed asthma was 7.6% vs 5.9% in nonexposed subjects ($p = 0.036$). In never-smokers without a family history of asthma, the prevalence of physician-diagnosed asthma in subjects reporting childhood ETS

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exposure was 6.8% vs 3.8% in nonexposed subjects ($p < 0.001$). Subjects with childhood ETS exposure were more likely to start smoking in adulthood. The prevalence of ever-smokers was 54.5% vs 33.8% ($p < 0.0001$) in nonexposed subjects. ETS was the most commonly reported LAWI in the total sample (21%), followed by exercise in cold air (20%), dust (19%), exercise (16%), perfume (15%), cold air (12%), pollen (10%), and pets (8%). All LAWIs were more frequently reported by women. CONCLUSIONS: Childhood exposure to ETS is associated with an increased prevalence of asthma among adult never-smokers, especially in nonatopic subjects. Children exposed to ETS are also more likely to become smokers. ETS is as a major LAWI.

Inspiratory Muscle Training in Patients with COPD: Effect on Dyspnea, Exercise Performance, and Quality of Life—Sanchez Riera H, Montemayor Rubio T, Ortega Ruiz F, Cejudo Ramos P, Del Castillo Otero D, Elias Hernandez T, Castillo Gomez J. Chest 2001 Sep;120(3):748-756.

OBJECTIVE: The aim of the study was to assess the effect of target-flow inspiratory muscle training (IMT) on respiratory muscle function, exercise performance, dyspnea, and health-related quality of life (HRQL) in patients with COPD. PATIENTS AND METHODS: Twenty patients with severe COPD were randomly assigned to a training group (group T) or to a control group (group C) following a double-blind procedure. Patients in group T ($n = 10$) trained with 60 to 70% maximal sustained inspiratory pressure (SIP_{max}) as a training load, and those in group C ($n = 10$) received no training. Group T trained at home for 30 min daily, 6 days a week for 6 months. MEASUREMENTS: The measurements performed included spirometry, SIP_{max}, inspiratory muscle strength, and exercise capacity, which included maximal oxygen uptake ($\dot{V}_{O_2}$), and minute ventilation ($\dot{V}_E$). Exercise performance was evaluated by the distance walked in the shuttle walking test (SWT). Changes in dyspnea and HRQL also were measured. RESULTS: Results showed significant increases in SIP_{max}, maximal inspiratory pressure, and SWT only in group T ($p < 0.003$, $p < 0.003$, and $p < 0.001$, respectively), with significant differences after 6 months between the two groups ($p < 0.003$, $p < 0.003$, and $p < 0.05$, respectively). The levels of $\dot{V}_{O_2}$ and $\dot{V}_E$ did not change in either group. The values for transitional dyspnea index and HRQL improved in group T at 6 months in comparison with group C ($p < 0.003$ and $p < 0.003$, respectively). CONCLUSIONS: We conclude that targeted IMT relieves dyspnea, increases the capacity to walk, and improves HRQL in COPD patients.

Inspiratory Muscle Strength in Acute Asthma—Stell IM, Polkey MI, Rees PJ, Green M, Moxham J. Chest 2001 Sep;120(3):757-764.

STUDY OBJECTIVES: The aim of this study was to measure inspiratory pressure-generating capacity in patients presenting with acute asthma, as it has been suggested that inspiratory muscle fatigue may contribute to breathlessness and acute respiratory failure. DESIGN: Descriptive study. SETTING: Emergency departments of two inner-city hospitals. PATIENTS: Fifty-one patients with acute asthma, and 45 patients without respiratory disease who served as control subjects. Measurements and results: Maximum inspiratory pressure-generating capacity was measured soon after presentation by the sniff nasal inspiratory pressure (SNIP) method. The mean (SD) SNIP was 110 cm H_2O (23 cm H_2O) in men with asthma (mean for control subjects, 126 cm H_2O [25 cm H_2O]; $p < 0.05$) and 80 cm H_2O [24 cm H_2O] in women with asthma (mean for control subjects, 105 cm H_2O (26 cm H_2O); $p < 0.01$). In a second study of simultaneous SNIP and intrathoracic pressure measurements in a group of patients with acute asthma ($n = 10$) and control subjects ($n = 11$), the effect of airways obstruction on SNIP was assessed. The measurement of sniff esophageal pressure was more negative than SNIP by approximately 16% in asthmatic patients and by 4% in control subjects. Taking account of the likely effect of airways obstruction on SNIP, the reduction in inspiratory pressure-generating capacity that was observed in these patients with moderately severe acute asthma was minor and was consistent with the modest hyperinflation observed. CONCLUSIONS: This study did not find evidence of inspiratory muscle weakness or fatigue in patients with moderately severe acute asthma presenting to the emergency department.

2 Years' Experience with Inspiratory Muscle Training in Patients with Neuromuscular Disorders—Koessler W, Wanke T, Winkler G, Nader A, Toifl K, Kurz H, Zwick H. Chest 2001 Sep;120(3):765-769.

PURPOSE: The aim of our study was to assess the long-term effects of specific inspiratory muscle training (IMT) in patients with neuromuscular disorders (NMDs) who have various degrees of respiratory impairment. Patients and methods: Twenty-seven patients with NMDs (Duchenne's muscular dystrophy, 18 patients; spinal muscular atrophy, 9 patients) underwent 24 months of IMT. Patients were divided into three groups according to their vital capacity (VC) values. VC was measured as the parameter for the respiratory system involvement of the disease. Maximal inspiratory pressure (PImax) was assessed as the parameter for respiratory muscle strength, and the results of the 12-s maximum voluntary ventilation test (12sMVV) were assessed as the parameter for respiratory muscle endurance. Pulmonary and inspiratory muscle function parameters were assessed 6 months before training, at the beginning of training, and then every 3 months. RESULTS: The PImax values improved in group A (VC, 27 to 50% predicted) from 51.45 to 87.00 cm H_2O, in group B (VC, 51 to 70% predicted) from 59.38 to 94.4 cm H_2O, and in group C (VC, 71 to 96% predicted) from 71.25 to 99.00 cm H_2O. The 12sMVV values improved in group A from 52.69 to 69.50 L/min, in group B from 53.18 to 62.40 L/min, and in group C from 59.48 to 70.5 L/min. For all three groups, there was a significant improvement of PImax ($p < 0.007$) and 12sMVV ($p < 0.015$) until the 10th month when a plateau phase was reached with no decline in the following month until the end of training. CONCLUSION: With IMT, respiratory muscle function can be improved in the long term of up to 2 years.

Predictors of Participation and Attendance in a New Asthma Patient Self-Management Education Program—Muntner P, Sudre P, Uldry C, Rochat T, Courteheuse C, Naef AF, Perneger TV. Chest 2001 Sep;120(3):778-784.

BACKGROUND: Low participation limits the effectiveness of patient education interventions. In this study, the characteristics of patients who agreed to participate in a clinical trial of disease self-management education for asthma were compared to the characteristics of those who declined, and among the former group patients who actually attended were compared to those who did not. METHODS: The education program, implemented at the Geneva University Hospitals between 1996 and 1998, consisted of three interactive sessions spread over 3 weeks. Only 131 of 253 eligible patients (52%) agreed to participate in the trial, and only 83 patients (63%) attended two to three educational sessions. All eligible patients filled out baseline questionnaires and were interviewed by a trained physiotherapist. RESULTS: Lower confidence in the patient's own current treatment regimen and a more severe baseline asthma attack were independently associated with participation in the trial. Among those who agreed to participate in the study, a university education, longer asthma duration, older age, and a higher level of asthma management knowledge were associated with higher attendance. Quality-of-life scores were not associated with higher course attendance. Among all eligible participants, persons with lower knowledge of asthma management (which was assessed by what to do during an asthma attack and knowledge of the correct use of a peak expiratory flowmeter and inhalers) were less likely to enroll in the trial and to attend the educational training sessions. CONCLUSIONS: Strategies need to be developed to motivate patients with lower disease self-management knowledge to participate in asthma education programs.

Cardiopulmonary Exercise Testing in Children with Heart Failure Secondary to Idiopathic Dilated Cardiomyopathy—Guimaraes GV, Bellotti G, Mocelin AO, Camargo PR, Bocchi EA. Chest 2001 Sep;120(3):816-824.

STUDY OBJECTIVE: To determine and compare the cardiopulmonary responses of healthy children and children with heart failure due to idiopathic dilated cardiomyopathy (IC) to progressive treadmill exercise testing. SETTING: University teaching hospital specializing in cardiology. PATIENTS OR PARTICIPANTS: Twenty-six children with stable, chronic heart failure (left ventricular ejection fraction < 45%) caused by IC (IC group) and 12 healthy children (control group). INTERVENTIONS: After 12-lead resting ECG, all children underwent progressive treadmill exercise testing using a modified Naughton protocol. Tests were performed in a controlled-temperature exercise facility, at least 2 h after a light meal. MEASUREMENTS AND RESULTS: Cardiopulmonary parameters were assessed at rest, at anaerobic threshold (AT), and at peak exercise. At rest, the tidal volume (V_T) and O_2 consumption ($\dot{V}_{O_2}$) for heart rate (O_2 pulse) were lower, while the heart rate, respiratory rate, and ventilatory equivalent for O_2 (minute ventilation [$\dot{V}_E$]/$\dot{V}_{O_2}$) were higher in the IC group compared with the control group. At AT, the systolic BP, O_2 pulse, V_T, exercise duration, $\dot{V}_{O_2}$, C_{O_2} production ($\dot{V}_{CO_2}$), and $\dot{V}_E$ were lower, while the $\dot{V}_E/\dot{V}_{O_2}$ and ventilatory equivalent for C_{O_2} ($\dot{V}_E/\dot{V}_{CO_2}$) were higher in the IC group ($p < 0.05$). At peak exercise, the IC group had a significantly lower systolic BP, O_2 pulse, $\dot{V}_E$, V_T, exercise duration, $\dot{V}_{O_2}$, and $\dot{V}_{CO_2}$, but higher $\dot{V}_E/\dot{V}_{O_2}$ and $\dot{V}_E/\dot{V}_{CO_2}$ than the control group ($p < 0.05$). The $\dot{V}_E/\dot{V}_{CO_2}$ slope was significantly higher for the IC group. No correlation existed between variables evaluated at rest vs during exercise. CONCLUSIONS: Gas exchange analysis performed during exercise successfully differentiated children with heart failure from healthy children.

Late Complications of Collapse Therapy for Pulmonary Tuberculosis—Weissberg D, Weissberg D. Chest 2001 Sep;120(3):847-851.

STUDY OBJECTIVES: Collapse therapy for pulmonary tuberculosis involved placement of various materials to occupy space and keep the lung collapsed. Complications are encountered decades later. PATIENTS AND METHODS: Between 1980 and 1997, we treated 31 patients with a history of pulmonary tuberculosis in whom collapse therapy had been used and who later developed complications related to their treatment. Pyogenic empyema was present in 24 patients, pleural calcifications with bronchopleural fistula was present in 3 patients, pleural calcification with nonresolvable pneumothorax was present in 1 patient, and migration of a foreign body with formation of subcutaneous mass occurred in 3 patients. All patients with empyema were treated with antibiotics and tube drainage of pus. In addition, Lucite balls were extracted in 4 patients, lung decortication was performed in 6 patients, thoracoplasty was performed in 2 patients, and fenestration was performed in 16 patients. Bronchopleural fistulas were closed with sutures and reinforced with intercostal muscle flap in three patients; in one patient with pleural calcification and nonresolvable pneumothorax, tube drainage was attempted. In three patients with subcutaneous mass due to paraffin migration, paraffin was extracted. RESULTS: Pulmonary decortication (six patients) and thoracoplasty (two patients) resulted in elimination of empyema. Extraction of Lucite balls resulted in lung expansion and elimination of empyema in three of four patients; draining sinus remains in one patient. Fenestration resulted in elimination of empyema in 12 of 16 patients, with 3 patients with residual draining sinuses and 1 patient with remaining empyema. All bronchopleural fistulas closed with intercostal muscle flap remained closed. Following extraction of paraffin blocks, infection developed in one patient. During the follow-up period, three patients died, all of unrelated causes. CONCLUSIONS: Delayed complications of collapse therapy for tuberculosis should be treated without delay. Pressure on adjacent structures or their erosion presents danger and mandates immediate extraction; however, there is no need for routine removal of every residual plombe. Further increase in the number of multiple-drug resistant strains may force the return of collapse therapy.

Effect of Continuous Positive Airway Pressure and Placebo Treatment on Sympathetic Nervous Activity in Patients with Obstructive Sleep Apnea—Ziegler MG, Mills PJ, Loredo JS, Ancoli-Israel S, Dimsdale JE. Chest 2001 Sep;120(3):887-893.

STUDY OBJECTIVES: We studied the effect of continuous positive airway pressure (CPAP) treatment on sympathetic nervous activity in 38 patients with obstructive sleep apnea. DESIGN: Randomized, placebo-controlled trial. SETTING: Patients underwent polysomnography on three occasions in a clinical research center, and had BP monitored over 24 h at home. All of the patients had sleep apnea with a respiratory disturbance index (RDI) > 15. INTERVENTIONS: The patients were randomized blindly to CPAP or placebo (CPAP at ineffective pressure) treatment. Measurements and results: Prior to therapy, the number of apneas and the severity of nocturnal hypoxia correlated significantly with daytime urinary norepinephrine (NE) levels, but not nighttime urinary NE levels. CPAP treatment lowered daytime BP from 99 ± 2 mm Hg to 95 ± 3 mm Hg (mean ± SEM) and nighttime BP from 93 ± 3 mm Hg to 88 ± 3 mm Hg. Placebo CPAP treatment decreased both day and night mean BP only 2 mm Hg. CPAP, but not placebo, treatment lowered daytime plasma NE levels by 23%, daytime urine NE levels by 36%, daytime heart rate by 2.6 beats/min, and increased lymphocyte β_2-adrenergic receptor sensitivity (all $p < 0.05$). The effect of CPAP treatment on nighttime urine NE levels and heart rate did not differ from placebo treatment. There was a suggestion of an effect of placebo CPAP treatment on nighttime measures, but not on daytime measures. CONCLUSION: We conclude that daytime sympathetic nervous activation is greater with more severe sleep apnea. CPAP treatment diminished the daytime sympathetic activation; the potential nighttime effect of CPAP treatment was obscured by a small placebo effect.

Impact of Different Criteria for Defining Hypopneas in the Apnea-Hypopnea Index—Manser RL, Rochford P, Pierce RJ, Byrnes GB, Campbell DA. Chest 2001 Sep;120(3):909-914.

OBJECTIVES: To explore the effect of using different scoring criteria for hypopneas in the scoring of polysomnographic studies: (1) by estimating the level of agreement between apnea-hypopnea index (AHI) scores derived from different scoring methods, and (2) by examining the effect on the point prevalence of disease using different threshold values of the AHI. DESIGN: Retrospective analysis of 48 diagnostic polysomnographic records. SETTING: Tertiary-hospital sleep-disorders clinic. MEASUREMENTS: AHIs were derived from three different methods for scoring hypopneas. The hypopnea definitions used incorporated different combinations and threshold values of respiratory signal changes in addition to differences in the requirement for associated oxygen desaturation or arousal. The level of agreement between different scoring methods was assessed by constructing Bland-Altman plots and calculating intraclass correlation coefficients (ICCs). κ statistics were used to assess agreement between the different methods using varying thresholds of AHI to categorize sleep apnea (AHI > 5, AHI > 15, and AHI > 20). RESULTS: The random-effects ICC for the three methods was 0.89, suggesting that the different scoring methods tended to rank patients fairly consistently. However, the point prevalence of disease estimated by using different thresholds of AHI was found to vary depending on the method used to score sleep studies (κ, 0.30 to 0.95). CONCLUSIONS: These findings have implications for case finding, population-prevalence estimates, and grading of disease severity for access to government-funded continuous positive airway pressure services. Guidelines for standardizing the measurement and reporting of sleep studies in clinical practice should be implemented.

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Sublingual Capnography: A Clinical Validation Study—Marik PE. Chest 2001 Sep;120(3):923-927.

OBJECTIVE: To compare sublingual P_{CO_2} (Psl_{CO_2}) measurements with gastric intramucosal P_{CO_2} (Pim_{CO_2}) as well as with the traditional indexes of tissue oxygenation in hemodynamically unstable ICU patients. DESIGN: A prospective, validation study. SETTING: The medical and coronary ICUs of a community teaching hospital. PATIENTS: Consecutive patients with severe sepsis, septic shock, or cardiogenic shock requiring pulmonary artery catheterization for hemodynamic management. INTERVENTIONS: During the first 24 h of ICU admission, the Psl_{CO_2}, Pim_{CO_2}, and blood lactate concentrations as well conventional hemodynamic and oxygenation parameters were recorded every 4 to 6 h. The Psl_{CO_2}-P_{aCO_2} and Pim_{CO_2}- P_{aCO_2} differences were used as indexes of tissue dysoxia. These variables were correlated with each other as well as with the traditional markers of tissue oxygenation. RESULTS: Seventy-six data sets were obtained on 22 patients. Fifteen patients had severe sepsis/septic shock, and 7 patients did not have sepsis. A patient with ischemic bowel who had a large Pim_{CO_2}- Psl_{CO_2} difference (60.2 mm Hg) was excluded. The initial Psl_{CO_2} and Pim_{CO_2} measurements were 43.5 ± 10.4 mm Hg and 42.8 ± 10.9 mm Hg, respectively (correlation coefficient [r] of 0.86; $p < 0.001$). The mean Psl_{CO_2} and Pim_{CO_2} for the entire data set were 48.0 ± 13.4 mm Hg and 46.1 ± 12.3 mm Hg, respectively ($r = 0.78$; $p < 0.001$). Ten patients died. The initial Psl_{CO_2}- P_{aCO_2} difference was 9.2 ± 5.0 mm Hg in the survivors and 17.8 ± 11.5 mm Hg in the nonsurvivors ($p = 0.04$). The initial Pim_{CO_2}- P_{aCO_2} difference was 8.4 ± 4.8 mm Hg in the survivors and 16.1 ± 13.7 mm Hg in the nonsurvivors ($p = 0.08$, not significant). The initial Psl_{CO_2}- P_{aCO_2} difference correlated with the initial mixed venous-arterial CO_2 gradient ($r = 0.66$; $p = 0.001$), but correlated poorly with the initial blood lactate concentration ($r = 0.38$), mixed venous P_{O_2} ($r = 0.05$), and systemic oxygen delivery ($r = - 0.39$). CONCLUSION: In this study, sublingual capnometry yielded measurements that correlated well with those of gastric tonometry. Psl_{CO_2} may serve as a technically simple and noninvasive clinical measurement of tissue dysoxia in critically ill and injured patients.

Predicting Mortality in Patients Suffering from Prolonged Critical Illness: An Assessment of Four Severity-of-Illness Measures—Carson SS, Bach PB. Chest 2001 Sep;120(3):928-933.

STUDY OBJECTIVES: Investigators have been using severity-of-illness indexes such as APACHE II (acute physiology and chronic health evaluation score II) to describe patients with prolonged critical illness. However, little is known about the utility of these indexes for this patient population. We evaluated the ability of four severity-of-illness indexes to predict mortality rates in 182 patients with prolonged critical illness. DESIGN: Retrospective inception cohort study. SETTING: A single, urban, long-term, acute-care hospital in Chicago. PATIENTS: One hundred eighty-two patients transferred from 37 acute-care hospital ICUs. Measurements and results: We assessed four indexes: the acute physiology and chronic health evaluation II, the simplified acute physiology score II, the mortality prediction model II, and the logistic organ dysfunction system using variables measured on admission to the long-term acute-care hospital ICU. We found that none of these indexes distinguished well between the patients who lived and the patients who died (area under ROC [receiver operating characteristics] curve < 0.70 for all), nor did they assign correct probabilities of death to individual patients (Hosmer-Lemeshow goodness-of-fit statistics, $p < 0.01$ for all). CONCLUSIONS: Investigators and clinicians should use caution in using severity-of-illness measures developed for acutely ill patients to describe critically ill patients admitted to long-term care units. As clinical practice and research focus more on these latter patients, development of adequately performing severity-of-illness measures appropriate to this patient population will be needed.

International Conference for the Development of Consensus on the Diagnosis and Treatment of Ventilator-associated Pneumonia—Rello J, Paiva JA, Baraibar J, Barcenilla F, Bodi M, Castander D, et al. Chest 2001 Sep;120(3):955-970.

Ventilator-associated pneumonia (VAP) is an important health problem that still generates great controversy. A consensus conference attended by 12 researchers from Europe and Latin America was held to discuss strategies for the diagnosis and treatment of VAP. Commonly asked questions concerning VAP management were selected for discussion by the participating researchers. Possible answers to the questions were presented to the researchers, who then recorded their preferences anonymously. This was followed by open discussion when the results were known. In general, peers thought that early microbiological examinations are warranted and contribute to improving the use of antibiotherapy. Nevertheless, no consensus was reached regarding choices of antimicrobial agents or the optimal duration of therapy. Piperacillin/tazobactam was the preferred choice for empiric therapy, followed by a cephalosporin with antipseudomonal activity and a carbapenem. All the peers agreed that the pathogens causing VAP and multiresistance patterns in their ICUs were substantially different from those reported in studies in the United States. Pathogens and multiresistance patterns also varied from researcher to researcher inside the group. Consensus was reached on the importance of local epidemiology surveillance programs and on the need for customized empiric antimicrobial choices to respond to local patterns of pathogens and susceptibilities.

The Effect of Incentive Spirometry on Postoperative Pulmonary Complications: A Systematic Review—Overend TJ, Anderson CM, Lucy SD, Bhatia C, Jonsson BI, Timmermans C. Chest 2001 Sep;120(3):971-978.

OBJECTIVE: To systematically review the evidence examining the use of incentive spirometry (IS) for the prevention of postoperative pulmonary complications (PPCs). METHODS: We searched MEDLINE, CINAHL, HealthSTAR, and Current Contents databases from their inception until June 2000. Key terms included "incentive spirometry," "breathing exercises," "chest physical therapy," and "pulmonary complications." Articles were limited to human studies in English. A secondary search of the reference lists of all identified articles also was conducted. A critical appraisal form was developed to extract and assess information. Each study was reviewed independently by one of three pairs of group members. The pair then met to reach consensus before presenting the report to the entire review group for final agreement. RESULTS: The search yielded 85 articles. Studies dealing with the use of IS for preventing PPCs ($n = 46$) were accepted for systematic review. In 35 of these studies, we were unable to accept the stated conclusions due to flaws in methodology. Critical appraisal of the 11 remaining studies indicated 10 studies in which there was no positive short-term effect or treatment effect of IS following cardiac or abdominal surgery. The only supportive study reported that IS, deep breathing, and intermittent positive-pressure breathing were equally more effective than no treatment in preventing PPCs following abdominal surgery. CONCLUSIONS: Presently, the evidence does not support the use of IS for decreasing the incidence of PPCs following cardiac or upper abdominal surgery.

Antipyretics: Mechanisms of Action and Clinical Use in Fever Suppression—Aronoff DM, Neilson EG. Am J Med 2001 Sep;111(4):304-315.

Fever is a complex physiologic response triggered by infectious or aseptic stimuli. Elevations in body temperature occur when concentrations of prostaglandin E_2 (PGE_2) increase within certain areas of the brain. These elevations alter the firing rate of neurons that control thermoregulation in the hypothalamus. Although fever benefits the nonspecific immune response to invading microorganisms, it is also viewed as a source of discomfort and is commonly suppressed with antipyretic medication. Antipyretics such as aspirin have been widely used since the late 19th century, but the mechanisms by which they relieve fever have only been characterized in the last few decades. It is now clear that most antipyretics work by inhibiting the enzyme cyclooxygenase and reducing the levels of PGE_2 within the hypothalamus. Recently, other mechanisms of action for antipyretic drugs have been suggested, including their ability to reduce proinflammatory mediators, enhance anti-inflammatory signals at sites of injury, or boost antipyretic messages within the brain. Although the complex biologic actions of antipyretic agents are better understood, the indications for their clinical use are less clear. They may not be indicated for all febrile conditions because some paradoxically contribute to patient discomfort, interfere with accurately assessing patients receiving antimicrobials, or predispose patients to adverse effects from other medications. The development of more selective fever-relieving agents and their prudent use with attention to possible untoward consequences are important to the future quality of clinical medicine.

Severe Pulmonary Embolism Associated with Air Travel—Lapostolle F, Surget V, Borron SW, Desmaizieres M, Sordelet D, Lapandry C, et al. N Engl J Med 2001 Sep 13;345(11):779-783.

BACKGROUND: Air travel is believed to be a risk factor for pulmonary embolism, but the relation between pulmonary embolism and distance flown has not been documented. The aim of this study was to investigate whether the duration of air travel is related to the risk of pulmonary embolism. METHODS: From November 1993 to December 2000, we systematically reviewed all cases of pulmonary embolism requiring medical care on arrival at France's busiest international airport. Data on the geographic origins of all flights and the numbers of passengers were collected in order to evaluate the incidence of pulmonary embolism per 1 million passenger arrivals as a function of the distance traveled. RESULTS: A total of 135.29 million passengers from 145 countries or other areas arrived at Charles de Gaulle Airport during the period of the study, of whom 56 had confirmed pulmonary embolism. The incidence of pulmonary embolism was much higher among passengers traveling more than 5000 km (3000 mi) (1.5 cases per million, as compared with 0.01 case per million among those traveling less than 5000 km). The incidence of pulmonary embolism was 4.8 cases per million for those traveling more than 10,000 km (6000 mi). CONCLUSIONS: A greater distance traveled is a significant contributing risk factor for pulmonary embolism associated with air travel.

Effects of Different Continuous Positive Airway Pressure Devices and Periodic Hyperinflations on Respiratory Function—Pelosi P, Chiumello D, Calvi E, Taccone P, Bottino N, Panigada M, et al. Crit Care Med 2001 Sep;29(9):1683-1689.

OBJECTIVE: To compare the effect on respiratory function of different continuous positive airway pressure systems and periodic hyperinflations in patients with respiratory failure. DESIGN: Prospective SETTING: Hospital intensive care unit. PATIENTS: Sixteen intubated patients (eight men and eight women, age 54 ± 18 yrs, P_{aO_2}/F_{IO_2} 277 ± 58 torr, positive end-expiratory pressure 6.2 ± 2.0 cm H_2O). INTERVENTIONS: We evaluated continuous flow positive airway pressure systems with high or low flow plus a reservoir bag equipped with spring-loaded mechanical or underwater seal positive end-expiratory pressure valve and a continuous positive airway pressure by a Servo 300 C ventilator with or without periodic hyperinflations (three assisted breaths per minute with constant inspiratory pressure of 30 cm H_2O over positive end-expiratory pressure). MEASUREMENTS AND MAIN RESULTS: We measured the respiratory pattern, work of breathing, dyspnea sensation, end-expiratory lung volume, and gas exchange. We found the following: a) Work of breathing and gas exchange were comparable between continuous flow systems; b) the ventilator continuous positive airway pressure was not different compared with continuous flow systems; and c) continuous positive airway pressure with periodic hyperinflations reduced work of breathing (10.7 ± 9.5 vs. 6.3 ± 5.7 J/min, $p < 0.05$) and dyspnea sensation (1.6 ± 1.2 vs. 1.1 ± 0.8 cm, $p < 0.05$) increased end-expiratory lung volume (1.6 ± 0.8 vs. 2.0 ± 0.9 L, $p < 0.05$) and P_{aO_2} (100 ± 21 vs. 120 ± 25 torr, $p < 0.05$) compared with ventilator continuous positive airway pressure. CONCLUSIONS: The continuous flow positive airway pressure systems tested are equally efficient; a ventilator can provide satisfactory continuous positive airway pressure; and the use of periodic hyperinflations during continuous positive airway pressure can improve respiratory function and reduce the work of breathing.

Physiologic Effects of Transtracheal Open Ventilation in Postextubation Patients with High Upper Airway Resistance—Uchiyama A, Mori T, Imanaka H, Nishimura M. Crit Care Med 2001 Sep;29(9):1694-1700.

OBJECTIVE: To investigate whether transtracheal open ventilation (TOV), pressure control ventilation (PCV) through a minitracheotomy tube (internal diameter 4 mm), is an effective method of inspiratory assistance under high upper airway resistance in postextubation patients; to compare, in a lung model study, TOV with other methods. DESIGN: Clinical study: A prospective, controlled, crossover study. Lung model study: A prospective laboratory trial. SETTING: Clinical study: A six-bed general intensive care unit in a teaching hospital. Lung model study: Animal research laboratory. PATIENTS: Clinical study: Eleven postextubation patients, who had undergone minitracheotomy for sputum retention between January 1997 and December 1997. SUBJECT: Lung model study: Two-bellows-in-a-box lung model, which included ordinary and high levels of upper airway resistance. INTERVENTIONS: Clinical study: Ventilatory settings were: assist/control (A/C) mode, 2 breaths/min of A/C back-up rate, 35-40 cm H_2O of PCV, 0.6-0.8 secs of inspiratory time, and 0 cm H_2O of positive end-expiratory pressure. The ventilatory parameters of TOV were compared with those of spontaneous breathing (SB). Lung model study: Effect of TOV on inspiratory assistance was compared with those of SB, open minitracheotomy, 5 L/min of transtracheal gas insufflation, and 5 and 10 cm H_2O of pressure support ventilation (PSV), which simulated noninvasive positive ventilation. TOV ventilatory settings were: A/C mode; 30, 40, and 50 cm H_2O of PCV, 0.9 secs of inspiratory time, and 0 cm H_2O of positive end-expiratory pressure. At each ventilatory setting, we adjusted the inspiratory effort of the model to give a tidal volume of 0.5 L. MEASUREMENTS AND MAIN RESULTS: Clinical study: TOV was performed for 76.6 ± 38.6 hrs (mean ± sd) over 5.6 ± 2.6 days without major complication. Peak tracheal pressure, which was measured distal to the minitracheotomy tube in six patients by a catheter pressure transducer, was 4.33 ± 0.59 cm H_2O. Inspiratory tidal volume delivered by the ventilator was 0.51 ± 0.06 L. Respiratory rate during TOV was lower than during SB. According to esophageal pressure and respiratory inductive plethysmography, TOV reduced the patient's inspiratory work and improved the breathing pattern. Lung model study: Mean tracheal pressure during TOV and 10 cm H_2O of PSV were positive values and they had larger inspiratory assistance according to the pressure-time product of pleural pressure. Although high upper airway resistance reduced the inspiratory assistance of PSV, it did not change the effects of TOV. CONCLUSIONS: TOV effectively reduced patient's inspiratory work and was more useful than open minitracheotomy and transtracheal gas insufflation. TOV also improved the breathing pattern. TOV may be useful for resolving some postextubation respiratory problems and avoiding the need for reintubation.

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5 Talking With Patients and Families About Death and Dying
6 Pressure vs. Volume Ventilation: Does It Matter?
7 Inpatient Management of COPD
8 High-Frequency Oscillatory Ventilation

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PROGRAM 1: Withholding and Withdrawing Life Support in the ICU

Gordon D. Rubenfeld, MD and Richard D. Branson, BA, RRT, FAARC

This presentation will give you a blueprint for dealing with the dying patient and their family members. It will teach you how to determine the proper time and method of addressing end of life. Plus, it details how management of end of life does not reside with a single caregiver but is part of the process for everyone involved in the patient's care.

Live Videoconference February 12, 11:30 a.m. – 1:00 p.m. Central Time
Teleconference with Video March 5, 11:30 a.m. – 12:00 Noon Central Time

PROGRAM 2: Weaning from Mechanical Ventilation: New Insights, New Guidelines

Neil R. MacIntyre, MD, FAARC and Dean R. Hess, PhD, RRT, FAARC

This program will help you to understand what conditions determine that a patient is ventilator dependent. Reviews evidence-based weaning guidelines and the keys to successful weaning. Teaches how you can expedite the weaning process and discontinuation of the ventilator.

Live Videoconference April 16, 11:30 a.m. – 1:00 p.m. Central Time
Teleconference with Video May 14, 11:30 a.m. – 12:00 Noon Central Time

PROGRAM 3: Neonatal and Pediatric Ventilators: What's the Difference?

Mark J. Heulitt, MD, FAARC, and Richard D.Branson, BA, RRT, FAARC

This session will give you an understanding of the critical differences between adults and children. Discussion will cover how and why the ventilator is triggered in this population; management of the work of breathing and physiologic differences; and ventilator design and the modes of artificial ventilation available.

Live Videoconference May 21, 11:30 a.m. – 1:00 p.m. Central Time
Teleconference with Video June 25, 11:30 a.m. – 12:00 Noon Central Time

PROGRAM 4: Ventilator Graphs: What's With That Wave?

Jon D. Nilsestuen, PhD, RRT, FAARC and Richard D. Branson, BA, RRT, FAARC

You will learn why checking a graphics display for critical markers is essential in proper utilization of waveforms. Plus, you will learn how to distinguish between machine breaths and patient pressure support breaths and how to use this information in ventilator adjustments. You will also learn about auto-PEEP and how to identify its presence on a graphics trace.

Live Videoconference July 16, 11:30 a.m. – 1:00 p.m. Central Time
Teleconference with Video August 13, 11:30 a.m. – 12:00 Noon Central Time

PROGRAM 5: Talking With Patients and Families About Death and Dying

Helen M. Sorensen, MA, RRT, FAARC and David J. Pierson, MD, FAARC

Learn how communication is a key to easing suffering at end of life and how to make dying easily understood by all parties. Also, learn how attitudes toward death vary among different ethnic groups and how to recognize the importance these differences play in termination of life support.

Live Videoconference August 20, 11:30 a.m. – 1:00 p.m. Central Time
Teleconference with Video September 17, 11:30 a.m. – 12:00 Noon Central Time

PROGEAM 6: Pressure versus Volume Ventilation: Does It Matter?

Robert S. Campbell, RRT, FAARC and Richard D. Branson, BA, RRT, FAARC

This program will give you a grasp of all the variables that enter into the decision to use pressure or volume ventilation. You will gain an understanding of the physiology of assisted breathing and how it is key to final selection of ventilatory mode. You will also learn what is displayed on ventilator screens and where to look for the information.

Live Videoconference September 10, 11:30 a.m. – 1:00 p.m. Central Time
Teleconference with Video October 8, 11:30 a.m. – 12:00 Noon Central Time

PROGRAM 7: Inpatient Management of COPD

Randall Rosenblott, MD and David J. Pierson, MD, FAARC

Learn the accepted guidelines for identifying and treating patients with COPD, including the therapeutic efficacy of steroids in the management of the acute exacerbation of COPD. You will also learn about respiratory failure and other potential complications that would require intervention in the patient's care.

Live Videoconference October 22, 11:30 a.m. – 1:00 p.m. Central Time
Teleconference with Video November 12, 11:30 a.m. – 12:00 Noon Central Time

PROGRAM 8: High-Frequency Oscillatory Ventilation

Thomas E. Stewart, MD and Richard D. Branson, BA, RRT, FAARC

Learn how proper ventilator management can preclude inflicting harm on the artificially ventilated patient. Plus, you will also gain an understanding of the conditions warranting HFOV, its potential complications, and how to identify the correct patient for this procedure.

Live Videoconference November 19, 11:30 a.m. – 1:00 p.m. Central Time
Teleconference with Video December 10, 11:30 a.m. – 12:00 Noon Central Time

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The Presenters

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Washington, Seattle, WA

Quality of Life Before Intensive Care Unit Admission and Its Influence on Resource Utilization and Mortality Rate—Rivera-Fernandez R, Sanchez-Cruz JJ, Abizanda-Campos R, Vazquez-Mata G. Crit Care Med 2001 Sep;29(9):1701-1709.

OBJECTIVE: To analyze the quality of life of critically ill patients before their intensive care admission and its relation to age, variables measured in the intensive care unit (ICU; severity of illness, therapeutic effort, resource utilization, and length of stay), and in-hospital mortality rate. DESIGN: Observational prospective multicenter study. SETTING: Eighty-six medical-surgical ICUs in Spain, including coronary patients. PATIENTS: We studied 8,685 patients between 1992 and 1993. Patients <16 yrs old and those dying within the first 6 hrs were excluded. MEASUREMENTS AND MAIN RESULTS: Data collection included age, gender, admission diagnosis, severity level by Acute Physiology and Chronic Health Evaluation (APACHE) III, quality of life survey score, therapeutic activity level by Therapeutic Intervention Scoring System (TISS), and ICU and hospital mortality rate. Pre-ICU quality-of-life score was 3.74 ± 4.42 points; 33.24% of patients had a normal quality of life (0 points), and numbers of patients declined logarithmically in relationship to increasing quality-of-life scores, with only 189 patients having a score >15 points. Pre-ICU quality-of-life score correlated with age ($r = 0.289$, $p < 0.001$), with severity level by APACHE III score ($r = 0.217$, $p < 0.001$), and weakly with TISS ($r = 0.067$, $p < 0.001$). There was no correlation between quality of life and length of ICU stay. Patients dying in hospital after ICU discharge ($n = 429$) had worse quality of life (5.88 ± 5.38 points) than those dying in the ICU ($n = 1,453$, 4.8 ± 4.94), who themselves had a worse quality of life than hospital survivors ($n = 6,803$, 5.05 ± 5.07; $p < 0.0001$ by analysis of variance), with significant differences between all three groups. In the multivariate analysis, pre-ICU quality-of-life was related to age, APACHE III score, and hospital mortality rate but not to TISS or ICU length of stay. Pre-ICU quality of life was introduced as a variable in the APACHE III prediction model and entered the model after acute physiology score, diagnosis, and age and before prior patient location and comorbidities. The area under the receiver operating characteristics curve was 0.834 when quality-of-life was included and 0.83 when not. CONCLUSIONS: In Spain, the quality of life of critically ill patients before their ICU admission is good, and only a small proportion of patients have a low quality of life before admission. Previous quality of life is related to hospital mortality rate but contributes very little to the discriminatory ability of the APACHE III prediction model and has little influence on ICU resource utilization as measured by length of stay and therapeutic activity.

Postextubation Fiberoptic Endoscopic Evaluation of Swallowing After Prolonged Endotracheal Intubation: A Randomized, Prospective Trial—Barquist E, Brown M, Cohn S, Lundy D, Jackowski J Crit Care Med 2001 Sep;29(9):1710-1713.

BACKGROUND: Critically ill trauma patients frequently require prolonged endotracheal intubation and ventilator support. After extubation, swallowing difficulties may exist in ≤ 50% of patients. We sought to determine whether performing a swallowing evaluation would reduce the incidence of postextubation aspiration and subsequent pneumonia. DESIGN: Randomized, prospective clinical trial of fiberoptic endoscopic evaluation of swallowing (FEES) vs. routine clinical management in patients after prolonged intubation. METHODS: Seventy patients who were intubated for > 48 hrs were randomized. FEES examinations were performed within 24 ± 2 hrs after extubation. Silent aspiration was defined as the appearance of liquid or puree bolus below the true vocal cords without coughing during a FEES examination. Clinical aspiration was defined as the removal of enteral content from below the vocal cords, usually during endotracheal tube placement. RESULTS: There were five episodes of aspiration and pneumonia in the FEES group (14%, two silent) and two in the clinical group (6%, not significant, Fisher exact test). Patients aged > 55 yrs and those with vallecular stasis on FEES examination were at significantly higher risk of postextubation aspiration. All patients with pneumonia had an associated aspiration episode. CONCLUSIONS: Patients with prolonged orotracheal intubation are at risk of aspiration after extubation. The addition of a FEES examination did not change the incidence of aspiration or postextubation pneumonia.

Factors Associated with Withdrawal of Mechanical Ventilation in a Neurology/Neurosurgery Intensive Care Unit—Diringer MN, Edwards DF, Aiyagari V, Hollingsworth H. Crit Care Med 2001 Sep;29(9):1792-1797.

OBJECTIVE: The objective of this study was to identify factors associated with the decision to withdraw mechanical ventilation from patients in a neurology/neurosurgery intensive care unit. Specifically, the following factors were considered: the severity of the neurologic illness, the healthcare delivery system, and social factors. DESIGN: Retrospective analysis of prospectively collected clinical database. SETTING: Neurology/neurosurgery intensive care unit of a large academic tertiary care hospital. PATIENTS: Patients were 2,109 nonelective admissions to the neurology/neurosurgery intensive care unit who received mechanical ventilation over a period of 82 months. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: The average age was 56 ± 19.7 yrs, 53% were male, and 81% were functionally normal before admission. The median Glasgow Coma Scale score was 14, the average Acute Physiology and Chronic Health Evaluation II severity of illness score was 13.5 ± 8.3, and probability of death was 18.2 ± 22.0%. Mechanical ventilation was withdrawn from 284 (13.5%). Factors that were independently associated with withdrawal of mechanical ventilation were as follows: more severe neurologic injury [admission Glasgow Coma Scale score (odds ratio 0.86/point, confidence interval 0.82-0.90), diagnosis of subarachnoid hemorrhage (odds ratio 2.44, confidence interval 1.50-3.99), or ischemic stroke (odds ratio 1.72, confidence interval 1.13-2.60)], older age (odds ratio 1.04/yr, confidence interval 1.03-1.05), and higher Acute Physiology and Chronic Health Evaluation II probability of death (odds ratio 1.03/%, confidence interval 1.02-1.04). Mechanical ventilation was less likely to be withdrawn if patients were African-American (odds ratio 0.50, confidence interval 0.36-0.68) or had undergone surgery (odds ratio 0.44, confidence interval 0.2- 0.67). Marital status, premorbid functional status, clinical service (neurology vs. neurosurgery), attending status (private vs. academic), and type of health insurance were not associated with decisions to withdraw mechanical ventilation. CONCLUSIONS: We conclude that decisions to withdraw mechanical ventilation in the neurology/neurosurgery intensive care unit are based primarily on the severity of the acute neurologic condition and age but not on characteristics of the healthcare delivery system. Care is less likely to be withdrawn from African-American patients or those who had surgery.

Pulse Oximetry in Sickle Cell Anemia—Fitzgerald RK, Johnson A. Crit Care Med 2001 Sep;29(9):1803-1806.

OBJECTIVES: To determine whether pulse oximetry is accurate and if it correlates with arterial blood gas saturation in pediatric patients with sickle cell anemia. DESIGN: Prospective, comparative study using a convenience sample of patients with sickle cell anemia who had simultaneous arterial blood gas sampling and pulse oximetry. SETTING: Children's Memorial Hospital, a large tertiary care pediatric hospital in Chicago, IL. Patients selected from the emergency department and the pediatric intensive care unit. PATIENTS: Twenty-four consecutive patients with sickle cell anemia who had simultaneous arterial blood gas sampling and pulse oximetry. MEASUREMENTS AND MAIN RESULTS: Twenty-four patients had a total of 70 simultaneous pulse oximeter and blood gas pair samples. Each patient's initial pulse oximeter/blood gas pair was used in the statistical analysis. Three patients had venous samples and were excluded from comparison, leaving 21 arterial

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blood gas/pulse oximeter pairs for analysis. The pulse oximeter correlated well with the cooximeter-measured arterial saturation (r^2 =0.74). The pulse oximeter significantly underestimated saturation by a mean of -1.6% (95% confidence interval, -0.3 to -3; p =0.03). CONCLUSIONS: Pulse oximetry correlates well with cooximeter-measured saturation in patients with sickle cell anemia. Pulse oximetry significantly underestimates true arterial saturation, but the bias is clinically insignificant. Pulse oximetry can be used reliably to estimate the arterial oxygen saturation in patients with sickle cell anemia.

Estimation of End-Expiratory Lung Volume Variations by Optoelectronic Plethysmography—Dellaca RL, Aliverti A, Pelosi P, Carlesso E, Chiumello D, Pedotti A, Gattinoni L. Crit Care Med 2001 Sep;29(9):1807-1181.

OBJECTIVE: To test the capability of optoelectronic plethysmography (OEP) to monitor positive end-expiratory pressure (PEEP)-induced changes of end-expiratory lung volume (EELV) changes in mechanically ventilated paralyzed patients. DESIGN: Laboratory and clinical investigation. SETTING: Intensive care unit of the Ospedale Maggiore Policlinico di Milano. PATIENTS: A total of eight patients with respiratory failure of various degrees, sedated and paralyzed. INTERVENTIONS: PEEP variations (±5 cm H_2O) relative to the baseline PEEP of 10 cm H_2O. MEASUREMENTS AND MAIN RESULTS: In the model protocol, we tested the reproducibility of the OEP by repeating volume measurements of a plastic torso model over a 21-hr period, every 30 mins. The variations of OEP measurements of the torso model (9337 mL value) were encountered in a range of 16 mL (sd = 4 mL). In the patient protocol, we measured the end-expiratory volume of the chest wall (EEVCW) breath-by-breath by OEP before, during, and after the PEEP increase/decrease and we compared its variations with the corresponding variations of EELV measured by helium dilution technique. The regression line between EELV changes measured by helium and EEVCW changes measured by OEP resulted very close to the identity line (slope 1.06, intercept -0.02 L, r^2 = 0.89) and their difference was not related to their absolute magnitude. After PEEP increase, the new steady state of EEVCW was reached approximately in 15 breaths; and, after PEEP decrease, in 3-4 breaths. The slow increase in EEVCW was mainly because of the abdominal compartment. CONCLUSION: OEP measurements of EEVCW accurately reflect the changes of EELV. Furthermore, OEP allows a continuous compartmental analysis, even during unsteady conditions.

Sleep Histories Are Seldom Documented on a General Medical Service—Namen AM, Landry SH, Case LD, McCall WV, Dunagan DP, Haponik EF. South Med J 2001 Sep;94(9):874-879.

BACKGROUND: Sleep disorders are common, but the frequency of sleep history documentation in hospitalized patients is unknown. METHODS: We reviewed 442 initial histories and physical examinations recorded by 122 house officers and 47 medical students in 208 consecutive general medicine ward patients. RESULTS: Any reference to sleep was recorded in only 18 patients (9%), including 12 of 141 (9%) with conditions associated with obstructive sleep apnea. Sleep histories were recorded more often in women (13% vs 4%) and less often than histories of cigarette smoking or alcohol use. Medical students recorded such histories more often than did house officers. Patients with sleep histories more often had pulse oximetry (78% vs 37%), pulmonary function testing (11% vs 1%), arterial blood gas analysis (67% vs 30%), or electrocardiograms (78% vs 49%). CONCLUSIONS: Sleep histories are documented infrequently in hospitalized patients. Patients with a recorded sleep history more often have tests that suggest increased concerns about cardiorespiratory risk and/or a different process of care.

Effect of Practice Variation on Resource Utilization in Infants Hospitalized for Viral Lower Respiratory Illness—Willson DF, Horn SD, Hendley JO, Smout R, Gassaway J. Pediatrics 2001 Oct;108(4):851-855.

Objective. Hospital care for children with viral lower respiratory illness (VLRI) is highly variable, and its relationship to severity and impact on outcome is unclear. Using the Pediatric Comprehensive Severity Index, we analyzed the correlation of institutional practice variation with severity and resource utilization in 10 children's medical centers. Methods. Demographics, clinical information, laboratory results, interventions, and outcomes were extracted from the charts of consecutive infants with VLRI from 10 children's medical centers. Pediatric Component of the Comprehensive Severity Index scoring was performed at admission and at maximum during hospitalization. The correlation of patient variables, interventions, and resource utilization at the patient level was compared with their correlation at the aggregate institutional level. Results. Of 601 patients, 1 died, 6 were discharged to home health care, 4 were discharged to rehabilitative care, and 2 were discharged to chronic nursing care. Individual patient admission severity score correlated positively with patient hospital costs (r = 0.48), but institutional average patient severity was negatively correlated with average institutional costs (r = -0.26). Maximal severity score correlated well with costs (r = 0.66) and length of stay (LOS; r = 0.64) at the patient level but poorly at the institutional level (r = 0.07 costs; r = 0.40 LOS). The institutional intensity of therapy was negatively correlated with admission severity (r = -0.03) but strongly correlated with costs (r = 0.84) and LOS (r = 0.83). Conclusions. Institutional differences in care practices for children with VLRI were not explained by differences in patient severity and did not affect the children's recovery but correlated significantly with hospital costs and LOS.

Randomized, Prospective Study of Low-Dose Versus High-Dose Inhaled Nitric Oxide in the Neonate With Hypoxic Respiratory Failure—Finer NN, Sun JW, Rich W, Knodel E, Barrington KJ. Pediatrics 2001 Oct;108(4):949-955.

Objective. There is little information on the response to very low doses of inhaled nitric oxide (iNO) in hypoxic near-term infants. The potential toxicities of iNO are dose related; thus, the ability to use lower doses safely and effectively may be advantageous. We hypothesized that there is no difference in the acute improvement in oxygenation between treatment with inhaled nitric oxide at 1 to 2 parts per million (ppm) or 10 to 20 ppm. Methods. We randomized near-term and term infants with hypoxic respiratory failure with oxygenation indices (OIs) of ≥10 and P_{aO_2} <100 on 2 separate blood gases taken at least 30 minutes apart. Infants with congenital diaphragmatic hernia were excluded. After parental consent was obtained, patients were randomized to receive a starting nitric oxide (iNO) dose of either 1 to 2 ppm (low-dose group, n = 15) or 10 to 20 ppm (high-dose group, n = 21). The response to iNO was assessed according to the increase in arterial P_{aO_2} and decrease in OI 30 to 60 minutes after exposure to the initial starting concentration. A response of <10% increase on P_{aO_2} and a <10% decrease in OI resulted in a doubling of iNO within the dose range protocol (1, 2, 4, and 8 ppm for the low-dose group; 10, 20, 40, and 80 ppm for the high-dose group). Results. Thirty minutes after the study gas was initiated, P_{aO_2} increased significantly overall in the low-dose (90.7 ± 41 torr to 166.8 ± 95.6 torr) and high-dose (76.2 ± 32.7 torr to 198.7 ± 142.8 torr) groups; the maximal increase was seen in the infants who initially were treated with 10 ppm. The OI ± also decreased significantly overall and also was significant in the high-dose group (21.0 ± 13.7 to 11.4 ± 10.4; low-dose: 18.3 ± 7.1 to 13.2 ± 12.3). There was a nonsignificant fall of P_{aCO_2} with iNO treatment (low dose 35 ± 7.3 to 30 ± 8.5 torr vs high dose 35.2 ± 9.9 to 32.4 ± 10.7 torr). A sustained response (ie, maintaining a P_{aO_2} and OI gain greater than 20% for the duration of the study gas administration) was greater in the high-dose group (53.3% vs 30.0%). In addition, dose increases were required more often in the low-dose group than in the high-dose group (80.0% vs

57.1%). Among patients who did not respond to the initial iNO dose, 100.0% and 83.3% responded at higher doses of iNO for the low- and high-dose groups, respectively. There were no differences for death, need for extracorporeal membrane oxygenation, or other outcomes between the groups. Conclusions. We did not find any significant difference in response to low- versus high-dose iNO. An initial exposure to low-dose iNO does not compromise the response to higher doses if required and may result in less toxicity.

Effects of the Dual Endothelin-Receptor Antagonist Bosentan in Patients with Pulmonary Hypertension: A Randomised Placebo-Controlled Study—Channick RN, Simonneau G, Sitbon O, Robbins IM, Frost A, Tapson VF, et al. Lancet 2001 Oct 6;358(9288):1119-1123.

BACKGROUND: Endothelin 1, a powerful endogenous vasoconstrictor and mitogen, might be a cause of pulmonary hypertension. We describe the efficacy and safety of bosentan, a dual endothelin-receptor antagonist that can be taken orally, in patients with severe pulmonary hypertension. METHODS: In this double-blind, placebo-controlled study, 32 patients with pulmonary hypertension (primary or associated with scleroderma) were randomly assigned to bosentan (62.5mg taken twice daily for 4 weeks then 125 mg twice daily) or placebo for a minimum of 12 weeks. The primary endpoint was change in exercise capacity. Secondary endpoints included changes in cardiopulmonary haemodynamics, Borg dyspnoea index, WHO functional class, and withdrawal due to clinical worsening. Analysis was by intention to treat. FINDINGS: In patients given bosentan, the distance walked in 6 min improved by 70 m at 12 weeks compared with baseline, whereas it worsened by 6 m in those on placebo (difference 76 m [95% CI 12-139], p=0.021). The improvement was maintained for at least 20 weeks. The cardiac index was 1.0 L min^{-1} m^{-2} (95% CI 0.6-1.4, pr0.0001) greater in patients given bosentan than in those given placebo. Pulmonary vascular resistance decreased by 223 dyn s cm^{-5} with bosentan, but increased by 191 dyn s cm^{-5} with placebo (difference -415 [-608 to -221], p=0.0002). Patients given bosentan had a reduced Borg dyspnoea index and an improved WHO functional class. All three withdrawals from clinical worsening were in the placebo group (p=0.033). The number and nature of adverse events did not differ between the two groups. INTERPRETATION: Bosentan increases exercise capacity and improves haemodynamics in patients with pulmonary hypertension, suggesting that endothelin has an important role in pulmonary hypertension.

The Assessment of Pulmonary Hypertension—McGoon MD. Clin Chest Med 2001 Sep;22(3):493-508.

The goals of evaluating pulmonary hypertension are detection, definition of severity and the nature of the hemodynamic lesion and its consequences, diagnosis of causal or associated conditions, and determination of optimal therapy. These objectives are reliably achieved by a disciplined approach employing multiple diagnostic tools. This chapter outlines the fundamental background and guidelines for assessing pulmonary hypertension, including consideration of several new and less frequently used methods to elucidate the physiologic mechanism. Since early detection and treatment may improve outcome, screening higher risk populations and a diagnostic approach to the milder spectrum of pulmonary hypertension is also addressed.

Medical Therapy of Pulmonary Hypertension: An Overview of Treatment and Goals—Barst RJ Clin Chest Med 2001 Sep:22(3):509-515.

Therapeutic medical advances over the past two decades have resulted in significant improvements in the outcome for patients with various forms of pulmonary arterial hypertension. As the current understanding of the pathology and pathobiology of pulmonary arterial hypertension has moved forward, rationale for additional therapeutic modalities with novel therapeutic agents has led to increased clinical investigations. A brief overview of the pathology and pathobiology is presented as background for an introduction to the current medical therapy for pulmonary arterial hypertension as well as the goals for future treatment.

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Medical Therapy of Pulmonary Hypertension: Conventional Therapies—Naeije R, Vachiery JL. Clin Chest Med 2001 Sep;22(3):5175-5127.

The 1-, 3-, and 5-year survival rates of the patients included in the National Institute of Health Registry on Primary Pulmonary Hypertension were 77%, 41%, and 27% respectively. It is unclear to what extent better applied conventional therapy contributes to improved survival rates that now are reported with calcium-channel blockers, prostacyclin, or even transplantation. To date, by far the most favorable results are reported with high-dose calcium-channel blockers combined with anticoagulant therapy, with survival rates at 3 years approximately 100%. It has to be emphasized, however, that such exceptionally favorable results are to be expected only in a small minority of patients who should not be considered to be cured because, sooner or later, their disease will continue to evolve. Further improvements obviously are needed for most patients with PAH. Interesting developments are likely in the coming years, with new multidrug approaches to control pulmonary vasoreactivity and remodeling and, hopefully, also with progress in lung transplantation. The past 2 decades have witnessed important progress in the treatment of PAH. Although significant improvements in quality of life and survival rate have been obtained with prostacyclin therapy, and better perspectives now are offered with atrial septostomy and lung transplantation, conventional therapy also has evolved. Patients now are counseled more adequately regarding how to remain physically active while avoiding exercise-induced anginal pain or syncope. Invasive and potentially risky medical procedures have been restricted in favor of noninvasive and functional evaluations whenever possible. Risk factors such as appetite suppressants, pregnancy, and hypobaric hypoxia are now better appreciated. The indications of supplemental oxygen, inotropic agents, and diuretics have been refined based on improved pathophysiologic understanding. Most patients now benefit from anticoagulant therapy with coumarin derivatives, although some uncertainty remains about the optimal international normalized ratio to be achieved. Safer acute reversibility testing now is performed with fewer and shorter-acting agents that are more specific to the pulmonary circulation to select the small proportion of patients who benefit from long-term high-dose calcium-channel blocker therapy.

Medical Therapy of Pulmonary Hypertension: The Prostacyclins—Galie N, Manes A, Branzi A. Clin Chest Med 2001 Sep;22(3):529-537.

Prostacyclin is a substance produced by endothelial cells that induces vasodilation and inhibition of platelet aggregation and of vascular cell migration and proliferation. A dysregulation of the prostacyclin metabolic pathways has been shown in patients with pulmonary arterial hypertension. The clinical use of prostacyclin has been made possible by the synthesis of stable analogues that possesses different pharmacokinetic properties but share similar pharmacodynamic effects. The greatest experience has been collected with intravenous epoprostenol while other compounds like subcutaneous UT-15, inhaled iloprost and oral beraprost are currently in different stages of clinical development. Although favorable results have been reported for each compound, different benefit-to-side effects profiles characterize the various modalities of the administration.

New and Experimental Therapies for Pulmonary Hypertension—Channick RN, Rubin LJ. Clin Chest Med 2001 Sep;22(3):539-545.

Advances in the understanding of the molecular and cellular pathogeneses of PPH have led clinicians beyond simple pulmonary vasodilation as the only treatment for PPH and to a realization that what were previously believed to be irreversible vascular lesions may, in fact, be reversible. The development of agents that target the known endothelial and nonendothelial defects in patients with PPH is well underway. Clinicians are witnessing an exciting new era for physicians and patients dealing with this disease.

Body Mass, Fat Percentage, and Fat Free Mass as Reference Variables for Lung Function: Effects on Terms for Age and Sex—Cotes JE, Chinn DJ, Reed JW. Thorax 2001 Nov;56(11):839-844.

BACKGROUND: Sex specific cross sectional reference values for lung function indices usually employ a linear model with terms for age and stature. The effects of also matching for body mass index (BMI = mass/stature^2) or its components, fat percentage of body mass (fat%) and fat free mass index (FFMI = fat free mass/stature^2) were studied. METHODS: The subjects were 458 asymptomatic male and female non-smokers (383 men) and 22 female ex-smokers. Measurements were made of ventilatory capacity, lung volumes, transfer factor (diffusing capacity, single breath CO method), and body composition (skinfold method). Linear and proportional regression models were used. RESULTS: Terms for fat% and FFMI significantly improved the accuracy of reference values for all the primary lung function indices. The improvements in subjects with atypical physiques (fat% and FFMI at the ends of the distributions for the subjects) were in the range 0.3-2.3 SD compared with conventional regression equations. The new partial regression coefficients on age were independent of age related changes in body fat. The coefficient for total lung capacity (TLC) on age in men was now positive. Most differences between the sexes were eliminated. A term for BMI improved the descriptions of subdivisions of TLC but lacked the other advantages. CONCLUSION: Allowance for fat% and FFMI increases the accuracy of reference equations for lung function, particularly for subjects with a lot of fat and little muscle or vice versa. Allowance for BMI is less informative.

Can the Increase in Body Mass Index Explain the Rising Trend in Asthma in Children?—Chinn S, Rona RJ. Thorax 2001 Nov;56(11):845-850.

BACKGROUND: The reported association between asthma and obesity and the documented rise in each over time have led to suggestions that rising obesity might explain the increase in the prevalence of asthma. Trends in both in British children participating in the National Study of Health and Growth were marked from 1982 to 1994. METHODS: Odd ratios for trends in asthma and symptoms in 8 and 9 year old children were calculated with and without adjustment for body mass index (BMI). RESULTS: In a representative sample of white children the odds ratio per year for asthma was 1.09 (95% CI 1.07 to 1.11) before and after adjustment for BMI for boys and 1.09 (95% CI 1.07 to 1.12) and 1.09 (95% CI 1.05 to 1.12), respectively, for girls. Unadjusted and adjusted odds ratios were also virtually identical for wheeze and "asthma or bronchitis". The lack of effect of adjustment was due to a change in the association between BMI and symptoms with time. CONCLUSIONS: Trends in overweight and obesity do not explain the increase in asthma. The evidence points towards the association between asthma and obesity being of recent origin. This may be explained by obesity being a marker of recent lifestyle differences now associated with both asthma and overweight.

Predicting Hypoxaemia During Flights in Children with Cystic Fibrosis—Buchdahl RM, Babiker A, Bush A, Cramer D. Thorax 2001 Nov;56(11):877-879.

BACKGROUND: We have previously suggested that it is possible to predict oxygen desaturation during flight in children with cystic fibrosis and chronic lung disease by non-invasive measurement of oxygen saturation following inhalation of 15% oxygen—the pre-flight hypoxic challenge. This study reports on the results of measurements over 5 years. METHODS: The study comprised a pre-flight hypoxic challenge measuring oxygen saturation by finger tip pulse oximetry (S_{pO_2}) during tidal breathing of 15% oxygen in nitrogen and spirometric testing 1 month before the flight followed by S_{pO_2} measurements during intercontinental flights to and from holidays abroad with children in wake and sleep states. RESULTS: Pre-flight tests were completed on 87 children with cystic fibrosis. Desaturation of <90% occurred in 10 children at some stage during the flight, three of whom received supplementary oxygen. Using a cut off S_{pO_2} of 90%, the pre-flight hypoxic challenge correctly predicted desaturation in only two of these children. The sensitivity and specificity of the pre-flight hypoxic challenge were 20% and 99%, respectively, compared with 70% and 96% for spirometric tests (using a cut off for forced expiratory volume in 1 second (FEV_1) of <50% predicted). Overall, pre-flight spirometric tests were a better predictor of desaturation during flight with the area under the Receiver Operating Characteristic (ROC) curve of 0.89 compared with 0.73 for the hypoxic challenge test. CONCLUSIONS: In this group of subjects pre-flight spirometric testing was a better predictor of desaturation during flight than the pre-flight hypoxic challenge.

Health Status Measurement in Chronic Obstructive Pulmonary Disease—Jones PW. Thorax 2001 Nov;56(11):880-887.

Health status measurement is a common feature of studies in chronic obstructive pulmonary disease (COPD). This review assesses recent evi-

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SATURDAY, Dec. 1

☐ 1. Keynote Address, D. Satcher
☐ 5. Tracking Flow of Residents, D.N. Muse
☐ 6. (6.) Role of Educators, E.A. Becker &
  (7.) Role of Managers, K.J. Stewart &
  (8.) Panel Discussion, M.Traband
☐ 9. Errors, Law and RCPs, A.L. DeWitt
☐ 10. Human Error: Changing Our Perceptions, J.W. Salyer
☐ 11. Patient Abuse in the Home: What Is It and What Are Your Responsibilities? D. Roberts
☐ 12. Assessing the Right Competencies for Home Care Therapists, S.L. Moreau
☐ 13. Discharging the Complex Pediatric Patient to the Home, J.P. Stegmaier
☐ 14. Does Economics Drive Home Care? R.W. McCoy
☐ 15. Surfactant Therapy, R.J. Rodriguez
☐ 16. Neonatal Update: Inhaled Nitric Oxide in the Neonate, S.R. Seidner
☐ 17. Mgt. Strategies for Prevention of BPD, R.J. Rodriguez
☐ 18. Overview of Dying and End-of-Life Care in America, P.A. Selecky
☐ 19. Withholding and Withdrawing Ventilation, R. Acevedo
☐ 20. Role of the Respiratory Therapist in Palliative Care, H.M. Sorenson
☐ 21. (21.) Building Coalitions, J.B. Fink
  (22.) Reaching Patients and Physicians with "Baylor's Rules of Two"!, G.E. Lawrence
☐ 23. (23.) Regional Asthma Center, L. Parish-Cooper
  (24.) Promoting Public Awareness: Successful Strategies, S. Blonshine
☐ 25. (25.) Sleep Disordered Breathing, M.B. Dunning III
  (26.) Protocols for Standardized Sleep Testing, R.N. Turner
☐ 27. (27.) New Polysomnograph Technologist Training Guidelines, R.N. Turner
  (28.) Survival Techniques for Shift Workers, M.B. Dunning
☐ 31 A. Issues & Trends in Allied Health Leadership, M. Harrington, Developing Your Career for Maximum Professional Effectiveness, M. W. Runge
  Breakout #1: Leadership in Clinical Practice, G. Gaebler
  Breakout #3: Leadership in Management, J.D. Kimble (Needs overtime tape)
☐ 31 B. Developing Professional Leadership, R. Krueger
  Success Stories, J.C. Bolden , D. Johnson
☐ 31 C. #2: Leadership in Clinical Research, A.B. Adams &
  #4: Leadership in Education, L. Van Scoder
☐ 34. Humor at the Bedside, M. Graves

SUNDAY, Dec. 2

☐ 35. Egan Lecture — Chronic Obstructive Pulmonary Disease - On the Exponential Curve of Progress, J.E. Heffner
☐ 36. Pulmonary Rehabilitation, B.W. Carlin
☐ 37. High Frequency Oscillatory Ventilation for ARDS: State of the Art 2001, S. Derdak
☐ 38. "The Ins and Outs" of Lung Transplantation, S.M. Levine MD, C.G. Durbin Jr.
☐ 39. Perspectives from Respiratory Care and Nursing, P. Carroll, & A.L. DeWitt Jr.
☐ 40. Risk Management and Respiratory Care, S.J. Price
☐ 41. Competency: Is Your Staff Ready? J.R. Edens
☐ 42. Managing Protocols Based on CPGs, E. Hoisington
☐ 45. A New Opportunity, C.M. Kercsmar
☐ 46. Questions for the Attorney, A.L. DeWitt
☐ 47. JCAHO: Showcasing Your Best, R.M. Ford
☐ 48. Justifying Human Resources: Best Use of a Valuable Asset, R.M. Ford
☐ 49. (49.) It's All Black and White, B. Yawn &
  (50.) Managing to Breathe via Internet, C. Olson
☐ 51. The Dirty Dozen, N. Sander
☐ 52. Selecting Clinical and Functional Outcomes in LTOT, T.L. Petty
☐ 53. Selecting Fiscal and Satisfaction Outcomes in LTOT, T.W. Bu
☐ 54. Measuring and Collecting Outcome Data, D.C. Shelledy
☐ 55. Using LTOT Outcome Data, R. Fary
☐ 56. Outcome Data Panel Discussion, T.W. Buckley, R. Fary, T.L. Petty, and D.C. Shelledy
☐ 57. Smoking Cessation, D.D. Gardner
☐ 58. New Strategies for Treating Tobacco Use and Dependence, Cohn
☐ 59. How Respiratory Care Managers Can Implement Tobacco Education Programs for Community-Wide Effect, S.M. Ciarl
☐ 60. Secondhand Smoke — What Can Health Care Professionals About It? A. French, B. Huffman
☐ 61. (61.) Evolution and Rationale of the Low VT Protocol, R. Br
  (62.) Practical Aspects of Implementing the Low VT Protoc Kallet
☐ 63. (63.) Can the ARDS Network Protocol Be Modified?, N.R. MacIntyre &
  (64.) How and Why to Use Recruitment Maneuvers in Low Ventilation, N.R. MacIntyre
☐ 65. (65.) Normal Mechanisms of Airway Clearance and Problen from the ICU to Home, B.K. Rubin &
  (66.) Positioning vs. Postural Drainage, J. Fink &
  (67.) Breathing Maneuvers, M. MacIllwaine
☐ 68. (68.) Positive Pressure Techniques for Airway Clearance, M Mahlmeister &
  (69.) High Frequency Oscillation of the Airway and Chest J. Fink &
  (70.) Airway Clearance and the Artificial Airways, R. Lewi
☐ 71. (71.) Pharmaceutic Approach to Airway Clearance, B.K. Rub
  (72.) Strategies for the Pediatric Patient, K.L. Davidson &
  (73.) Airway Clearance Strategies for the Vent Patient at Ho C. Lapin
☐ 74. RSV: Management and Treatment Advances, C.M. Kercsma
☐ 75. Test Your Skills on the State of the Profession, M.F. Traban
☐ 76. How to Survive as a Multi-Department Manager, S.J. Price
☐ 79. Technological Advances in Noninvasive Respiratory Monit G. Devine
☐ 80. Monitoring on the General Floor: What's the Future Going Like? P.T. Sharkey
☐ 81. A Proposal for Evidence-Based Practice in Neonatal Resuscitation, W.D. Rich
☐ 82. Classifying Asthma Patients through Symptom Analysis, T. Kallstrom
☐ 83. How Not to Run a Respiratory Care Service, K.L. Shrake

MONDAY, Dec. 3

☐ 84. Kittredge Lecture — Mechanical Ventilation: How Did We Here and Where Are We Going?, R.D. Branson
☐ 85. Intrapulmonary Percussive Ventilation, C. Diaz
☐ 88. Exercise Training: Are You Training Your Patients at the Ri Exercise Target? B.W. Carlin
☐ 89. Water Exercise in Pulmonary Rehabilitation Programs, M.W.
☐ 90. The Impact of the Institute of Medicine's Report for Respir Care Providers, S.P. Giordano
☐ 91. Evidence-Based Respiratory Care, D.J. Pierson
☐ 92. Managing Chronic Medical Conditions in the New Care De Framework, P.J. Dunne
☐ 93. (93.) Applying Case Management Principles in Home Care Stegmaier &
  (94.) Developing a Cost Model For Delivery of LTOT, T.W. B
☐ 95. (95.) What I Wish All Home Care Therapists Knew, B. Roger
  (96.) LTOT Utilization: The Bigger Picture! G. Spratt
☐ 97. (97.) Modifying Treatment Plans For the Aging Lung, T.S. LeGrand &
  (98.) Seeing Health Care through the Eyes of the Elderly, F Sorenson

- ☐ 99. (99.) Caring for the Older Pneumonia Patient, T.S. LeGrand & (100.) Senior Pulmonary Assessment, H.M. Sorenson
- ☐ 101. Interpretation of PFTs by RCPs, J.O. Nilsestuen
- ☐ 102. Results of a National Study, J.M. Boyle
- ☐ 103. Agency Updates ñ Through the eyes of the AARC, ARCF, CoARC and NBRC, C.P. Wiezalis, M.T. Amato, M. Welch Jr, and J. Long-Goding
- ☐ 104. Munchausen by Proxy, D. Roberts
- ☐ 105. Opening the Black Box during Mechanical Ventilation, M. Amato
- ☐ 107. (107.) Documenting Respiratory Practice Beyond the USA, J. Long-Goding H.L. Garza & (108.) Comparison of Two Methods for Administration of Inhaled Salbutamol, H.L. Molina
- ☐ 109. (109.) The Brazilian Experience, L.G. Ghion & (110.) The United Kingdom Experience, A. Hynes
- ☐ 111. (111.) The Italian Experience, S. Thompson & (112.) The Japanese Experience, H. Etchuya
- ☐ 113. (113.)The North America Experience, A. King & (114.) The Personal Experience — A Patient's View, B. Rogers, & Panel Discussion
- ☐ 115. Creating an Effective Multi-Cultural Work Environment, K.L. Shrake
- ☐ 116. Bronchiolitis Care Path, J.W. Salyer
- ☐ 117. Pediatric Asthma: Success with Therapist-Driven Protocols, T.R. Myers
- ☐ 118. Developing a Pediatric Consult Program, J.W. Salyer
- ☐ 119. Lung Protective Strategies for Status Asthmaticus, M.K. Brown
- ☐ 120. Acute Care of the Adult Asthmatic, J.I. Peters
- ☐ 121. Bronchodilator Resuscitation in the ER, J. Fink
- ☐ 122. Case Presentations of Pulmonary X-Rays, C.G. Durbin
- ☐ 123. (123.) P/V Curves Should Be Routinely Used in Ventilatory Management of ALI, K. Hargett, R.M. Kacmarek & (124.) Heliox is the Front-Line Treatment for Management of Acute Asthma, T.R. Myer, C.M. Kercsmar
- ☐ 125. New Modes of Mechanical Ventilation Are Necessary for Management of Patients with ARF, N.R. MacIntyre, R.D. Branson
- ☐ 126. Oxygen Toxicity in the ICU Is a Myth, D.J. Pierson, C.G. Durbin Jr
- ☐ 131. An Answer to Respiratory Care Re-Engineering, D.C. Oberly
- ☐ 132. What's Right and What's Wrong with Cardio-Pulmonary Exercise Tests, M.W. Millard
- ☐ 133. The Amazing History of Pulmonary Medicine, G.W. Lantz
- ☐ 134. New Uses for an Old Therapy, M.K. Brown

TUESDAY, Dec. 4

- ☐ 135. Which One for ARDS? M. Amato
- ☐ 136. What It Is and How You Can Help, R.R. Fluck
- ☐ 137. Prospective Payment System (PPS)
- ☐ 138. Models of Success for RCPs, K.A. Cornish
- ☐ 139. Wave Form Analysis, J.O. Nilsestuen
- ☐ 140. Diagnostic Testing: Pre- and Post-Lung Transplant, C.M. Fos
- ☐ 141. Lung Transplantation from the Patient's Perspective, M. Pierce
- ☐ 142. Apples to Apples: First Line Therapy, S. Jenkinson
- ☐ 143. Safety of First Line Options, T.A. Mahr,
- ☐ 144. Advantages of Combination Therapy, J. Bloom
- ☐ 145. Advances in Delivery: Does Particle Size Matter? T.A. Mah
- ☐ 146. NPPV Without Quantifiable Evidence: The Legal and Medi Ramifications, P.K. Blakely
- ☐ 147. Using Protocols in Respiratory Home Care, G. Spratt
- ☐ 148. Telemedicine and the Home Care Respiratory Therapist, P. Blakely
- ☐ 149. Corporate Compliance Plan: What the OIG Is Really Sayin Dunne
- ☐ 150. (150.) How To Come Up with a Good Research Question, Durbin Jr & (151.) How to Get a Research Project Done in Your Depart J. Ward
- ☐ 152. (152.) How to Write an Open Forum Abstract That Will Be Accepted, D.J. Pierson & (153.) How to Make an Effective Poster for Presentation at Open Forum, D.C. Shelledy & (154.) How to Prepare and Deliver an Effective Oral, Sum of Your Project, R.S. Campbell
- ☐ 155. Pulmonary Hypertension and the Respiratory Therapist, R. Rosenblatt
- ☐ 156. Management of Amyotrophic Lateral Sclerosis, C.E. Jackso
- ☐ 157. Insight to the Profession, Panel
- ☐ 158. Weaning from Mechanical Ventilation, N.R. MacIntyre
- ☐ 159. Treatment of the Adult Patient with Cystic Fibrosis, R.L. Rosenblatt
- ☐ 160. Recent Developments in the Management of Meconium Aspiration, R. Castro
- ☐ 161. Critical Diagnostic Thinking for Respiratory Therapists, D. Shelledy
- ☐ 164. Pharmacology and Patient Safety, J.H. Eichhorn
- ☐ 165. Non-invasive Monitoring during Procedural Sedation, D.H. Walker
- ☐ 166. Procedural Sedation in the ER: The Role of the Respiratory Therapist, B. Krauss,
- ☐ 167. Airway Remodeling: To Do or Not To Do? N.A. Hanania
- ☐ 168. Neonatal Critical Care Transport, H. Heiman
- ☐ 169. Neonatal Transport Cases, S. Segovia
- ☐ 170 A&B (2 Tapes) Allergic Disorders: The Child with Rhinitis Asthma, B. Martin
- ☐ 171. What's New in CPR ALS? T.A. Barnes
- ☐ 172. Recentralized Respiratory Services: Ten Things We Learne from Our Customers, G.F. Ellis
- ☐ 173. A Respiratory Therapist Could Have Saved President Georg Washington, D.J. Pierson

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dence for the validity of these measurements and their role as measures of the overall impact of the disease on the patient's daily life and wellbeing. It reviews the mostly widely used COPD specific questionnaires and examines the contribution that they make to an assessment of the overall effect of treatment. Finally, it addresses the question of how symptomatic benefit may be assessed in individual patients in routine practice.

Forced Inspiratory Nasal Flow-Volume Curves: A Simple Test of Nasal Airflow—Hooper RG. Mayo Clin Proc 2001 Oct;76(10):990-994.

OBJECTIVE: To observe and describe normal and abnormal inspiratory nasal flow-volume patterns. PATIENTS AND METHODS: In this observational case series, individuals with and without nasal symptoms underwent forced inspiratory nasal flow-volume (FINFV) curve measurements. The participants were volunteer adults from the staff and patients of a pulmonary subspecialty private practice office. To examine the flow patterns from the FINFV curves, definitions of normal and abnormal were established. Normal curves were defined as those from participants who had no nasal symptoms and a peak inspiratory nasal flow greater than 2.5 L/s. Abnormal curves were defined as those from participants who had 1 or more nasal symptoms, a peak inspiratory nasal flow lower than 2.5 L/s, and normal oral inspiratory flow. RESULTS: Study participants consisted of 10 staff and 58 patients. Fourteen individuals (21%) met the definition of normal and had FINFV curves that mimicked the shapes of normal oral flow-volume curves; 39 (57%) met the definition of abnormal and had FINFV curves that mimicked the patterns of abnormal oral flow-volume curves. The abnormal curves showed both fixed (33/39 [85%]) and variable (6/39 [15%]) patterns of obstruction. Fifteen participants (22%) did not meet either established definition. CONCLUSIONS: Forced inspiratory nasal flow-volume curves are a potentially useful clinical tool to measure nasal airflow. Normal and abnormal flow patterns are easily identifiable.

Evidence of a Current and Lasting National Anesthesia Personnel Shortfall: Scope and Implications—Schubert A, Eckhout G, Cooperider T, Kuhel A. Mayo Clin Proc 2001 Oct;76(10):995-1010.

OBJECTIVES: To prove the existence of a current anesthesiologist shortage, and to project the balance of labor supply and demand in the future. METHODS: To quantify the current supply we used published health personnel data from federal agencies and the American Medical Association, as well as membership data from the American Society of Anesthesiologists. We estimated anesthesiologist supply in 2001 based on the number of graduating residents and fellows, taking into account the loss of a portion of graduating residents due to temporary visa status. We assumed that neither a shortage nor an oversupply existed in 1994 and that demand for anesthesiologists was approximated by the number of surgical procedures reported by federal agencies. In modeling future supply and demand for anesthesiologists, we assumed that the current health care policy and economic climates will continue. We extrapolated demand using 1.5% to 3% yearly growth rates based on a synthesis of recent and projected procedure growth rates, procedure rates for the elderly, and population aging trends. We estimated the supply for 2001 through 2003 based on the current resident cohort modified by their projected graduation rate. Accounting for attrition during residency and the effect of fellowship training, we assumed that after 2003 the number of American medical graduates will initially increase by 15% annually and that the number of international medical graduates will decrease to a stable level of 500 trained each year. We assumed an average retirement age of 65 years. RESULTS: Our model suggests that there is currently a 3.6% to 10.9% shortage of anesthesiologists nationwide, depending on the assumption of a 2% or 3% increase in annual demand since 1994 and a constant pattern of work distribution by anesthesia providers. This amounts to approximately 1200 to 3800 anesthesiologists. If projected demand continues to increase at the rate of 1.5% to 2% annually, the shortfall will amount to 2.6% to 12.0% of the labor supply by 2005, representing a deficit of 1000 to 4500 anesthesiologists. By 2010, this shortfall is projected to disappear or continue to amount to about 11% of the anesthesiologist supply, depending on the assumptions about the rate of demand for anesthesiologists. Compared with the expected graduating class of 1100 anesthesiology residents in 2001, our model calls for nearly 1600 graduates by 2005 and 2000 by 2010. CONCLUSION: A substantive shortfall of anesthesia personnel exists in 2001 and will continue for years to come, fueled by changing population demographics, population health trends, and accelerating advancements in surgical technology, as well as growth in ambulatory and office-based surgery, pain medicine, and intensive care. In addition to focusing on financing, national health policy needs to address the adequacy of health care personnel resources for an aging population, in particular when they require surgery, are afflicted by painful conditions, or become critically ill.

Costeffectiveness of Diagnostic Tests—Mushlin AI, Ruchlin HS, Callahan MA. Lancet 2001 Oct 20;358(9290):1353-1355.

We review the principles underlying cost-effectiveness analysis of diagnostic tests and procedures. We use two clinical examples, diagnostic testing for early multiple sclerosis and for Helicobacter pylori to illustrate the methods of analysis and to show how the results can be useful for physicians or payers of health services in making decisions about provision and use of diagnostic services. Economic assessments of diagnostic tests are inherently more difficult than assessments of therapeutic interventions, mainly because of uncertainty about the relation between diagnosis and end results (outcomes) of care. Nonetheless, because of the increasing importance of diagnostic technology in medicine and healthcare, only with such assessments will the most value be gained from restricted medical resources.

Treatment of Obstructive Sleep Apnoea with Nasal Continuous Positive Airway Pressure in Stroke—Wessendorf TE, Wang YM, Thilmann AF, Sorgenfrei U, Konietzko N, Teschler H. Eur Respir J 2001 Oct;18(4):623-629.

The prevalence of obstructive sleep apnoea (OSA) following stroke is high and OSA is associated with increased morbidity, mortality and poor functional outcome. Nasal continuous positive airway pressure (nCPAP) is the treatment of choice for OSA, but its effects in stroke patients are unknown. The effectiveness and acceptance of treatment with nCPAP in 105 stroke patients with OSA, admitted to rehabilitation was prospectively investigated. Subjective wellbeing was measured with a visual analogue scale in 41 patients and 24-h blood pressure was determined in 16 patients before and after 10 days of treatment. Differences were compared between patients who did and did not accept treatment. There was an 80% reduction of respiratory events with concomitant increase in oxygen saturation and improvement in sleep architecture. No serious side-effects were noticed. Seventy-four patients (70.5%) continued treatment at home. Nonacceptance was associated with a lower functional status, as measured by the Barthel Index, and the presence of aphasia. Ten days after initiation of nCPAP, compliant users showed a clear improvement in wellbeing (differences in visual analogue scale (ΔVAS) mean±SD 26±26 mm) versus noncompliant patients (ΔVAS 2±25 mm, $p=0.021$). Only the compliant group had a reduction in mean nocturnal blood pressure (ΔBP; -8±7.3 mm Hg versus 0.8±8.4 mm Hg, $p=0.037$). Stroke patients with obstructive sleep apnoea can be treated effectively with nasal continuous positive airway pressure and show a similar improvement and primary acceptance to obstructive sleep apnoea patients without stroke. Continuous positive airway pressure acceptance is associated with improved wellbeing and decreased nocturnal blood pressure.

Propofol Infusion Is Associated with a Higher Rapid Shallow Breathing Index in Patients Preparing to Wean from Mechanical Ventilation

Mohammad Khamiees MD, Yaw Amoateng-Adjepong MD PhD, and Constantine A Manthous MD

OBJECTIVE: To determine whether propofol affects spontaneous breathing patterns in critically ill patients recovering from respiratory failure during initial attempts at liberation from mechanical ventilation. DESIGN: Observational cohort study. PATIENTS: Ten critically ill patients in the medical intensive care unit of a 300-bed community teaching hospital. MEASUREMENTS: Demographic and physiologic variables, including respiratory frequency and minute volume, were recorded while patients breathed on continuous positive airway pressure (of 5 cm H_2O) during and 20–30 min after cessation of propofol infusion. The ratio of respiratory frequency to tidal volume (rapid shallow breathing index or RSBI) was computed for both sets of measurements and values measured during and after propofol infusion were compared. RESULTS: The mean (± SEM) age was 54.0 ± 5.2 years and the mean (± SEM) APACHE II (Acute Physiology and Chronic Health Evaluation) score was 18.4 ± 2.0. During propofol infusion, patients breathed with a significantly lower tidal volume (0.245 vs 0.342 L, $p = 0.006$), higher RSBI (155.6 vs 114.8 breaths/min/L, $p = 0.004$), and tended to breathe more rapidly (34.3 vs 31.7 breaths/min, $p = 0.18$) than at 20–30 min after stopping propofol infusion. Three of 10 patients had RSBIs that were unfavorable (> 105 breaths/min/L) for weaning while on propofol but that became favorable (< 105 breaths/min/L) 20–30 min following cessation of propofol. The weight-adjusted dose of propofol was not correlated with the changes in any of the variables. CONCLUSIONS: Propofol causes changes in breathing pattern that could lead a caregiver to erroneously conclude that a patient is not ready to begin spontaneous breathing trials. Since this effect has also been noted following benzodiazepine infusion, the clinician should consider the patient's "sedation history" when using RSBI to guide weaning decisions. *Key words: mechanical ventilation, respiratory failure, weaning, liberation, rapid shallow breathing index, RSBI, respiratory rate, frequency, tidal volume, breathing pattern, sedatives, benzodiazepine, propofol.* [Respir Care 2002;47(2):150–153]

Introduction

The unassisted ratio of respiratory rate to tidal volume (f/V_T—the rapid shallow breathing index or RSBI) is one of the most reproducible and accurate[1–3] tools to expedite weaning of mechanically ventilated patients.[4] Recent reports have suggested that excessive sedation is associated with unnecessarily prolonged mechanical ventilation and intensive care unit length of stay.[5] Parenteral administration of benzodiazepines has been associated with increased respiratory rate and reduced V_T in human subjects.[6,7] However, no studies have examined the effects on breathing pattern (RSBI) of stopping prolonged sedative infusions in critically ill patients. In this study we examined the effects of stopping continuous propofol infusions on respiratory variables.

Methods

This study was approved by our hospital's investigational review board and was exempted from requiring in-

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Mohammad Khamiees MD, Yaw Amoateng-Adjepong MD PhD, and Constantine A Manthous MD are affiliated with Pulmonary and Critical Care, Bridgeport Hospital, Yale University School of Medicine, New Haven, Connecticut.

A version of this report was presented by Mohammad Khamiees MD at the May 2001 meeting of the American Thoracic Society, San Francisco, California.

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Table 1. Respiratory Variables During CPAP Breathing*

Variable	Before			After			p
	Mean ± SD	Median	Range	Mean ± SD	Median	Range	
RR (breaths/min)	34.3 ± 1.9	33.5	27–47	31.7 ± 2.6	30	23–48	0.18
V_T (L)	0.245 ± 0.024	0.251	0.107–0.352	0.342 ± 0.046	0.345	0.146–0.633	0.006
RSBI (breaths/min/L)	155.6 ± 19.3	143.3	88–261	114.8 ± 21.8	81.6	47–259	0.004

CPAP = continuous positive airway pressure
*Data from 10 patients just before and 20–30 min after cessation of propofol infusions.
RR = respiratory rate
V_T = tidal volume
RSBI = rapid shallow breathing index

formed consent from patients. This was a convenience sample of mechanically ventilated patients in our medical-cardiac intensive care unit between September 1999 and July 2000, who were receiving propofol for > 12 h, and whose physicians had asked that infusion be stopped to initiate weaning. The patient also had to be triggering the ventilator consistently over the set respiratory rate while in the assist control mode. In our intensive care unit, weaning is guided by a nonmandatory protocol that is executed by bedside nurses, respiratory therapists, and resident-trainees overseen by one of 4 board-certified intensivists. Patients who are no longer receiving vasopressors or inotropes and whose P_{aO_2}-F_{IO_2} ratio (ratio of arterial partial pressure of oxygen to fraction of inspired oxygen) is > 120 are assessed with 2–3 min of unassisted breathing through the endotracheal tube, with or without continuous positive airway pressure. There is no stipulation in the protocol regarding the degree of sedation during that measurement. A patient whose observed RSBI is < 125 breaths/min/L usually undergoes a spontaneous breathing trial via T-piece, continuous positive airway pressure or pressure support of ≤ 7 cm H_2O for 0.5–2 h. A patient whose RSBI is > 125 breaths/min/L undergoes a pressure support trial or is placed back on full ventilatory support.

Demographic data were recorded from the medical records. A single observer (CAM) measured the respiratory rate by counting patient breaths on physical examination during a minute of 5 cm H_2O continuous positive airway pressure (no pressure support) breathing. To allow breathing patterns to stabilize, 1–2 min of spontaneous breathing were allowed before measurements. All measurements were performed with the head of the bed at roughly 30°, while the patient inspired ≤ 50% oxygen (same as during assist control), and without verbal coaching. No medications affecting respiratory drive were given between measurements. Also recorded, at the end of the minute of unassisted breathing, was the minute ventilation from the digital display of the ventilator (Puritan Bennett 7200, Puritan Bennett/Tyco Healthcare, Pleasanton, California, which was the only ventilator used in the study). The manufacturer's description indicates that that minute ventilation value is "based on an 8-breath projected running average or a 1-minute sample, whichever comes first." The value was divided by the observed respiratory rate in order to generate better time-averaged V_T than by simply recording V_T from the digital display. The observed respiratory rate was then divided by the computed average V_T to yield the RSBI.

Each patient was studied once, and the values of respiratory rate, V_T, and RSBI before and after cessation of propofol were compared by paired Student's *t* tests. Regression analyses were performed to determine whether the weight-adjusted dose of propofol was associated with changes in respiratory frequency, V_T, and RSBI. Statistical significance was taken as $p < 0.05$.

Results

We studied 10 patients with a variety of medical illnesses. The mean (± SEM) age was 54.0 ± 5.2 y and the mean (± SEM) admission APACHE II (Acute Physiology and Chronic Health Evaluation) score was 18.4 ± 2.0. Seven patients were ventilated for hypoxemic and 3 for hypercapnic respiratory failure; 7 were being treated for pneumonia, 1 had a pulmonary embolism, 1 had an exacerbation of chronic obstructive pulmonary disease, and 1 had an asthma exacerbation. Patients had been intubated for an average of 8.0 ± 3.1 d and had been receiving propofol for 87.5 ± 25.8 h at an average dose of 41 μg/kg/min at the time of the study. Table 1 lists respiratory variables recorded during and after cessation of propofol infusions. Minute volume increased significantly (from 8.4 to 10.5 L/min, p = 0.046) and there was a statistically significant increase in computed V_T and decrease in RSBI following cessation of propofol. Respiratory frequency tended to decrease, but the change was not statistically significant (see Table 1). The magnitudes of these changes were *not* linearly correlated with the weight-adjusted doses of propofol infusion (Fig. 1). No important cardiopulmonary complications (excessive tachycardia, hypotension, or oxygen desaturation) were noted during measurement of RSBI in these patients. However, 1 patient had recorded minute volume of < 4 L/min both during and following propofol infusions.

Discussion

This study indicates that intravenous propofol, used to maintain comfort and patient-ventilator synchrony in these critically ill patients, is associated with rapid shallow breathing. The magnitude of this abnormality was *not* correlated with the weight-adjusted dose of propofol infusion, but the small sample precludes any definitive conclusions regarding the dose-response of propofol and breathing pattern.

Previous studies have indicated that patients receiving benzodiazepines for procedures breathe more rapidly and shallowly than at baseline.[6,7] However, one study showed no changes in respiratory variables following *low-dose* boluses of propofol.[8] To our knowledge, no previous studies have examined the effects of stopping continuous infusion of propofol (or benzodiazepines) on breathing pattern. So, even though this is the first study to indicate that propofol induces rapid shallow breathing in critically ill patients, this finding is not unexpected. We chose to study propofol rather than benzodiazepine because the duration of benzodiazepine's effect following discontinuation is erratic and can be prolonged.[5,9] Owing to its rapid onset and brief duration of action and the brief period of study (20–30 min), it is quite likely that the observed respiratory effects were related to propofol infusion and not to some other concurrent pathophysiologic event.

Although these findings are consistent with previous studies of benzodiazepines, they are of substantial importance to the care of critically ill patients. The RSBI is a highly validated tool[1–3] now used in many centers to guide initiation of spontaneous breathing trials. Moreover, in an important clinical study, the RSBI was used as the lynchpin of a weaning protocol that, when applied by respiratory therapists, reduced the duration of mechanical ventilation.[4] So if the RSBI is used to determine when to begin spontaneous breathing trials and sedatives affect breathing pattern, *residual effects of sedation are likely to impede the weaning process* and probably help explain why excessive sedation has been associated with prolonged mechanical ventilation.[5] Since even short-acting benzodiazepines can be associated with prolonged effects after cessation of continuous infusion,[9,10] it is possible, or even likely, that those medications have prolonged effects on respiratory pattern, which could impede expeditious weaning, especially when the RSBI is used to initiate and judge the success of trials. For example, in our sample of 10 patients, 3 had RSBIs that were unfavorable (> 105 breaths/min/L) while they received propofol but were favorable only 20–30 min following termination of the infusion. One of those patients

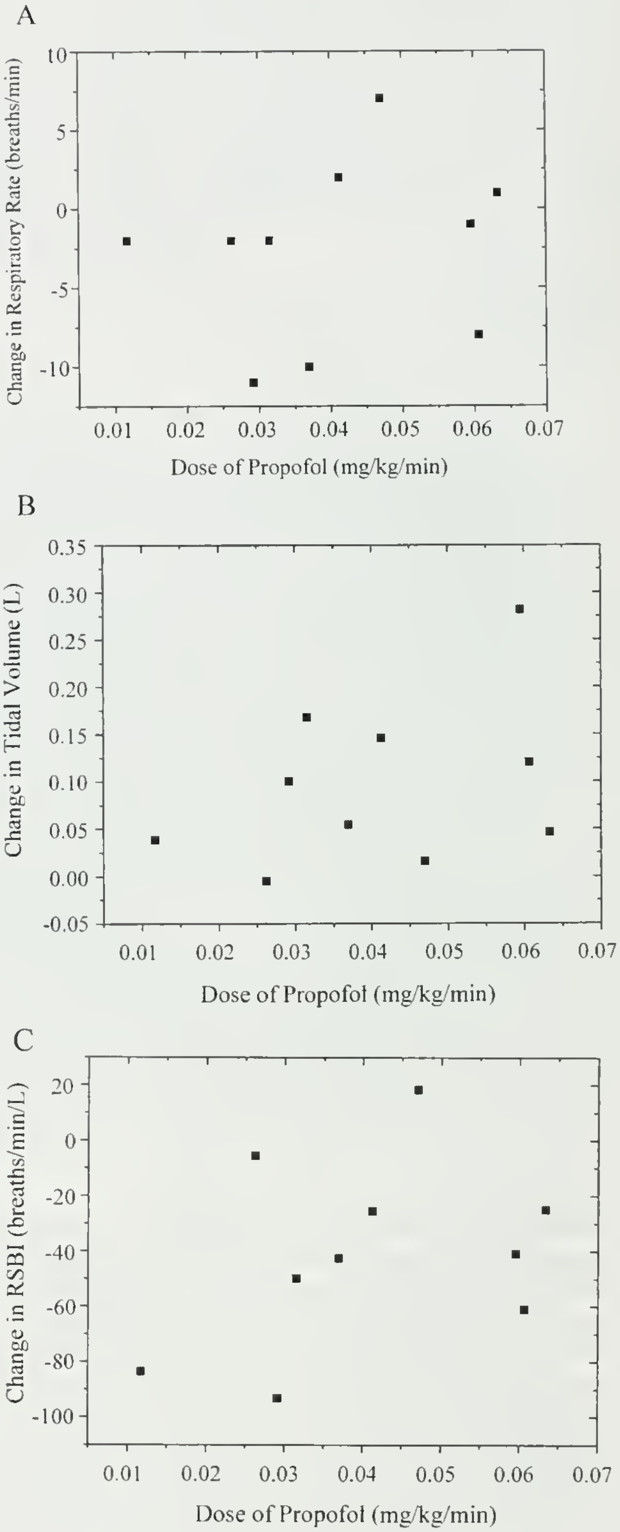

Fig. 1. Relationships of weight-adjusted propofol dose to change in respiratory variables. A: Change in respiratory rate. B: Change in tidal volume. C: Change in rapid shallow breathing index.

was successfully extubated on the same day despite an initial RSBI (on propofol) of > 105 breaths/min/L.

Conclusions

Infusion of propofol was associated with rapid shallow spontaneous breathing among patients recovering from respiratory failure. When the RSBI is used to guide weaning from mechanical ventilation, clinicians should be aware that the RSBI may be affected if sedatives have recently been administered.

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Treatment of Patients Hospitalized for Exacerbations of Chronic Obstructive Pulmonary Disease: Comparison of an Oral/Metered-Dose Inhaler Regimen and an Intravenous/Nebulizer Regimen

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OBJECTIVE: Compare the therapeutic efficacy of an oral/metered-dose inhaler (oral/MDI) regimen to an intravenous/nebulizer (I.V./neb) regimen of methylprednisolone, cefuroxime, and inhaled albuterol and ipratropium bromide in patients hospitalized for exacerbations of chronic obstructive pulmonary disease (COPD). DESIGN: Randomized, nonblinded, therapeutic trial. SETTING: Two community hospitals in Bangor, Maine. PATIENTS: 34 individuals with severe COPD. The mean admission forced expiratory volume in the first second was 0.75 L (oral/MDI 0.78 L, I.V./neb 0.71 L). RESULTS: Baseline demographic, laboratory, comorbidity, and ventilatory values determined in 19 patients who received the oral/MDI regimen and 15 patients treated with the I.V./neb regimen indicated comparability of the two groups. Outcome variables that compared oral/MDI to I.V./neb, including mean change in forced expiratory volume in the first second (0.12 L vs 0.13 L), mean length of stay (4.3 vs 5.1 d), and treatment failures (32% vs 33%), showed no significant differences. CONCLUSION: Patients hospitalized for COPD exacerbations can be successfully (and potentially less expensively) treated with an oral/MDI treatment regimen. *Key words: metered-dose inhaler, MDI, nebulizer, chronic obstructive pulmonary disease, COPD, exacerbation, intravenous, inhaled, methylprednisolone, cefuroxime, albuterol, ipratropium bromide.* [Respir Care 2002;47(2):154–158]

Introduction

Chronic obstructive pulmonary disease (COPD), a disorder characterized by airflow obstruction and/or mucus hypersecretion, is a major cause of morbidity and the fourth leading cause of mortality in the United States.[1] Periodic exacerbations are common, and patients are often hospitalized when they develop increasing dyspnea, progressive gas exchange impairment, or fail to respond to an outpatient therapeutic regimen.[1] Annual related health care costs in the United States are $15 billion, and hospitalization is the major component of those expenditures.[2]

Standard therapy for COPD exacerbations is well known and includes inhaled β_2 sympathomimetics and cholinergic agents, corticosteroids, xanthines, and antibiotics.[3] Demands on nursing and respiratory care services often exceed availability. Despite the magnitude of this problem, there have been relatively few clinical trials that clearly prove the efficacy of the dosing regimens or route by which they should be administered.[4–8] The present study was conducted to determine if comparable therapeutic results could be achieved among patients hospitalized for COPD exacerbations using a less resource-intensive regimen (oral medications and metered-dose inhaler [oral/MDI]) than conventional therapy (intravenous drugs and nebulizer [I.V./neb]).

Methods

Patients with acute COPD exacerbations admitted to Eastern Maine Medical Center and St Joseph Hospital com-

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munity-based medical centers in Bangor, Maine, during the period from February 1996 to April 1997 were considered for the study protocol. Eligibility was determined by:

- Chronic airflow obstruction (forced expiratory volume in the first second [FEV_1] < 60% of predicted), or
- FEV_1/forced vital capacity < 60% following bronchodilators, and
- Post-bronchodilator FEV_1 increase of < 15%, and
- Willingness to participate at the time hospitalization was necessary, following an increase of dyspnea, cough, or sputum production, plus one or more of:

1. Inadequate symptomatic response to outpatient management
2. Marked decrease in exercise capacity
3. Inability to sleep or eat due to dyspnea
4. Worsening hypoxemia, defined as $P_{aO_2} < 65$ mm Hg on room air, after correction for hyperventilation, assuming a respiratory quotient of 0.8 and new or worsening hypercarbia ($P_{aCO_2} > 44$ mm Hg with pH < 7.38 for the first time or $P_{aCO_2} > 50$ mm Hg with pH < 7.35).

Excluded from the study were patients with acute pneumonia (lobar or segmental infiltrate on chest radiograph), status asthmaticus, bronchiectasis, cystic fibrosis, upper airway obstruction, left ventricular dysfunction with an ejection fraction < 40%, positive blood culture, treatment with bi-level positive airway pressure or continuous positive airway pressure, endotracheal intubation, or inability to cooperate with MDI therapy via AeroChamber or mask inhalation.

A core group of respiratory therapists familiar with the study protocol admitted prospective patients, who were then randomized to either the oral/MDI regimen or conventional (I.V./neb) therapy. After informed consent was obtained, each patient underwent a ventilatory dynamic study (Vmax 20C, Sensormedics Corporation, Yorba Linda, California) and was given an initial bronchodilator treatment. Baseline demographic characteristics were recorded, along with a standard physical examination and laboratory values (complete blood count, screening urinalysis, chemistry profile, arterial blood gas values, chest radiograph, sputum culture, and blood culture for temperature > 102.5° F). Patients were monitored daily to determine ventilatory dynamics, oxygen saturation, level of dyspnea (Borg scale), quantity of inhaled bronchodilators, and length of hospital stay.

Patients were randomly assigned to either an oral/MDI regimen or the conventional I.V./neb regimen. The oral/MDI regimen was:

- Methylprednisolone: 40 mg per os (po) every 6 h until wheeze free, then 40 mg po every day.
- Albuterol: 1 puff initially administered at 30 s intervals over 2 min, and then 1 puff every 1 min, up to a maximum of 20 puffs every 4 h and every 1 h as needed until dyspnea was alleviated or the patient perceived that symptomatic baseline ventilatory status had been achieved.
- Ipratropium bromide: 4 puffs initially administered at 30 s intervals over 2 min, and then 1 puff every 1 min for a total of 8 puffs every 4 h and every 1 h as needed.
- Cefuroxime: 500 mg po twice a day unless the sputum culture was negative or sputum smear showed < 25 white blood cells per high-power-field. Trimethoprim/sulfa double-strength 1 po was administered twice a day if the patient was intolerant of cefuroxime or the organism was not sensitive.

The I.V./neb regimen consisted of:

- Methylprednisolone: 40 mg intravenously every 6 h until wheeze free and then 40 mg po every day.
- Nebulized 2.5 mg albuterol and 0.5 mg ipratropium bromide every 4 h while awake and every 1 h as needed.
- Cefuroxime: 1.5 g intravenously every 8 h until afebrile (temperature < 100° F) for 36 h, and then 500 mg po twice a day. Trimethoprium/sulfa double-strength 1 po was administered twice a day if the patient was intolerant of cefuroxime or the organism was not sensitive.

Nebulized medication was delivered via an Airlife Mistyneb nebulizer (Allegiance Healthcare, McGraw, Illinois). The MDI was used with an AeroChamber (Monaghan Medical, Plattsburgh, New York). Patients who were taking theophylline on admission continued to receive the drug as an oral preparation, with the level adjusted to achieve > 8 and < 16 mg/dL. Oxygen was adjusted to achieve > 88% saturation. Medications for patients with comorbid conditions were continued at their pre-admission doses, as warranted in accordance with the clinical circumstances.

Treatment failure was characterized as:

A. Minor: Patient or physician subjectively chose to employ the alternative regimen, either because of perceived dyspnea or treatment adverse effects without evidence of measurable clinical decline as defined in the moderate or major failure categories.

B. Moderate: Any of the following: (1) Development of respiratory distress (respiratory rate > 40 breaths/min for > 30 min), (2) Decrease in oxygen saturation > 10% below admission saturation or oxygen saturation < 85% despite supplemental oxygen, or (3) P_{aCO_2} increase of > 10 mm Hg above admission P_{aCO_2}.

C. Major: Either (1) necessity for continuous assisted mechanical ventilatory assistance with or without endotracheal intubation or (2) death.

Patients were discharged at the discretion of the attending physician when all of the following criteria were achieved:

1. Inhaled bronchodilator therapy use did not exceed every 4 h.
2. Previously ambulatory patient could walk across a room.

Table 1. Baseline Characteristics of Patients Treated for COPD Exacerbations

	Oral/MDI ($n = 19$)	I.V./Neb ($n = 15$)	p
Demographics			
Mean age (y)	67	71	0.09*
Gender (% male)	74	73	1.0†
Mean body mass index (kg/m^2)	24.5	23	0.47*
Resides > 20 miles from hospital (%)	26	20	1.0‡
Care provider at home (%)	67	67	1.0†
Comorbidities			
Cancer (%)	32	15	0.26‡
Diabetes (%)	26	7	0.20‡
Respiratory Status			
Current or former smoker (%)	84	93	1.0‡
Smoking > 45 pack-years (%)	32	53	0.20†
Uses > 2 respiratory medications (%)	84	67	0.42†

COPD = chronic obstructive pulmonary disease
MDI = metered-dose inhaler
I.V. = intravenous
Neb = nebulizer
*by Student's *t* test
†by Mantel-Haenszel chi-square test
‡by Fisher's exact 2-tail chi-square test

3. Patient was able to eat and sleep without frequent awakenings caused by dyspnea.
4. Reactive airway disease was judged to be stable.
5. Patient was assessed to be clinically stable, essentially wheeze-free and had not required parentaral therapy for > 12 h.
6. Arterial blood gas values were stable for > 12 h.
7. Patient (or home caregiver) understood the use and administration of medications.
8. Discharge follow-up plans were complete.

Statistical analysis was performed with a commercially available software package (Statistical Analysis System, SAS Institute, Cary, North Carolina). Both descriptive and outcomes data were analyzed using the Mantel-Haenszel chi-square test (except for the small cell sizes, where the Fisher's exact test was employed) for categorical parameters and the 2-sample *t* test for continuous parameters.[9] Statistical significance was taken as $p < 0.05$.[10]

The study was approved by the investigational review boards of both participating hospitals.

Results

Fifty patients were randomized and 34 of them completed the study. Among the 16 patients not analyzed (4 from the oral/MDI group and 12 from the I.V./neb group), 5 voluntarily withdrew, 4 left on physician request, and 7 were disqualified because of protocol failures. Thirty were admitted to Eastern Maine Medical Center and 4 to Saint Joseph Hospital. The number of patients who completed the study represents 29% (34 of 118) of the total number of individuals with COPD exacerbations admitted to both hospitals during the study period. There were 19 patients in the oral/MDI group and 15 in the I.V./neb group. One patient was admitted twice and one was admitted 3 times. They were randomized on study entry and were considered to be independent subjects for statistical purposes.

Table 1 shows the baseline demographics, comorbidities, and respiratory values. Table 2 shows the on-admittance laboratory values. Table 3 shows the outcome variables. Most of the study subjects had severe airway obstruction (mean FEV$_1$ 0.75 L, range 0.35–2.02 L). The

Table 2. Admission Laboratory Data of Patients Treated for COPD Exacerbations

	Oral/MDI ($n = 19$)	I.V./Neb ($n = 15$)	p
WBC > 10,800 (%)	16	13	1.0*
Temperature > 98.6° F (%)	32	27	1.0*
Sputum culture positive (%)	11	33	0.20*
Hgb < 12 g/dL (%)	32	40	0.61†
Mean FEV$_1$ (L)	0.78	0.71	0.42‡
pH	7.416 ± 0.052 (range 7.30–7.53)	7.412 ± 0.045 (range 7.33–7.46)	0.83*
Pa$_{CO_2}$ > 45 mm Hg (%)	21	40	0.28*
Pa$_{O_2}$ < 100 mm Hg (%)	79	80	1.0*
HCO$_3$ > 26 mEq/dL (%)	42	53	0.52†

COPD = chronic obstructive pulmonary disease
MDI = metered-dose inhaler
I.V. = intravenous
Neb = nebulizer
WBC = white blood cell count
Hgb = hemoglobin
FEV$_1$ = forced expiratory volume in the first second
*by Fisher's exact 2-tail chi square test
†by Mantel-Haenszel chi-square test
‡by Student's *t* test

Table 3. Outcome Variables of Patients Treated for COPD Exacerbations

	Oral/MDI (n = 19)	I.V./Neb (n = 15)	p
Mean FEV_1 (L)	0.96	0.93	< 0.82*
Mean change in FEV_1 (L)	0.12	0.13	< 0.91*
Mean length of stay (d)	4.3	5.1	< 0.56*
Treatment failure (%)	32	33	1.0†
Reduction in dyspnea (Borg scale)	1.56	1.77	0.75*

COPD = chronic obstructive pulmonary disease
MDI = metered-dose inhaler
I.V. = intravenous
Neb = nebulizer
Hgb = hemoglobin
*by Student's t test
†by Mantel-Haenszel chi-square test

oral/MDI group's mean FEV_1 was 0.78 L and the I.V./neb group's was 0.71 L. That difference is not statistically significant. None of the major outcome variables showed a significant difference, including mean change in FEV_1, length of stay, degree of dyspnea relief, and frequency of treatment failure. All treatment failures were minor (a change from one regimen to the other based on patient or physician preference), and treatment failure occurred with equal frequency in each group. The mean length of stay favored the oral/MDI regimen (4.3 vs 5.1 d), but the difference was not statistically significant.

The total dose of albuterol inhaled in the first 24 h averaged 45.5 puffs, whereas the total dose of ipratropium bromide used was 43.6 puffs. In each 24 h period thereafter, 37.2 puffs of albuterol and 40.9 puffs of ipratropium bromide were used. The maximum number of puffs used for any treatment was 20 of albuterol and 8 of ipratropium bromide. The average number of puffs per treatment was 7 for albuterol and 7.5 for ipratropium bromide. Pulse rates after bronchodilator inhalation showed no significant change from baseline values (increases were < 10 beats/min). The number of nebulizer treatments during the first 24 h was 6.3 and averaged 5.3 daily thereafter. Pulse rate increases > 10 beats/min were not seen following nebulizer therapy.

Discussion

This was a clinical study conducted under operational conditions in 2 community hospitals. Because it was designed to examine COPD exacerbations, patients with airway hyperreactivity, pneumonia, acute ventilatory failure, or those requiring ancillary respiratory support (bi-level positive airway pressure or continuous positive airway pressure) were specifically excluded in an effort to keep the study population as homogeneous as possible. Nonetheless, this investigation has several evident limitations. A number of patients could not be enrolled because of the logistics of trying to conduct research and deliver patient care simultaneously. As a result, 58% (68 of 118) of potential candidates were not studied, for a variety of reasons (staffing deficiencies 31, physician refusals 24, and patient refusals 13). Careful review of patient records, however, did not reveal any important departures from the therapy protocols among the patients analyzed.

Although a number of studies have been performed to determine the causes of COPD exacerbations, it is clear that infection alone is often not the major culprit.[11–16] Several epidemiological studies have suggested an association between indoor air pollution, home dampness, and respiratory symptoms.[17–20] Thus, it is possible that an important component to successful treatment may simply be removing patients from their home environments to minimize their exposure to inhalational irritants such as cigarette smoke, fumes, allergens, and dust. If that were true, then a therapeutic regimen that did not require the use of intensive medical resources could be administered in an alternative, appropriately supervised, nonhospital setting.

Conclusion

Despite the considerable difficulties and complexity involved in conducting this trial, the outcome indicated no significant differences between the 2 groups. This suggests that it may be feasible to treat COPD exacerbations with a less complicated and potentially less expensive regimen than is currently being employed in many hospitals. Because of the small number of patients in this initial trial, further research involving a more substantial number of patients would be necessary to amplify these initial observations, if the premise of this study is to be confirmed.

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Dry Powder Ipratropium Bromide Is As Safe and Effective As Metered-Dose Inhaler Formulation: A Cumulative Dose-Response Study in Chronic Obstructive Pulmonary Disease Patients

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A multi-center, open, randomized, 2-way crossover study was conducted with chronic obstructive pulmonary disease (COPD) patients to compare the safety and efficacy of cumulative doses of ipratropium bromide administered from a pressurized metered-dose inhaler (MDI) or from a breath-activated dry powder inhaler (DPI). Enrolled in the study were 39 patients with moderate to severe COPD and who showed a ≥ 15% increase in baseline forced expiratory volume in the first second (FEV_1) after 80 μg of ipratropium bromide. Thirty-six patients were evaluable for efficacy analysis, and 38 patients were included in the safety analysis group. A significant improvement in pulmonary function was observed following inhalation of cumulative doses of ipratropium bromide (from 20 to 320 μg), but no statistically significant difference was found between the 2 formulations. The dose-response curves were similar. There was no statistical difference in area-under-the-curve during the 180 min period after the last dose for any of the pulmonary function variables. Overall, effects on pulse rate, blood pressure, and QT interval on electrocardiogram were no different between the devices. Six mild adverse events occurred in 4 patients: ventricular ectopic beats on electrocardiogram at 270 min with MDI, bad taste with both MDI and DPI, slight transient increase in blood pressure in the same patient during each study day with both MDI and DPI. Two moderate adverse events occurred in 2 patients: transient ventricular ectopic beats on electrocardiograms with DPI at 270 min, moderate bronchospasm with MDI at 200 min. Patients expressed a preference for DPI, which was found to have a better acceptability and appeared to be easier to use than MDI. The new lactose powder formulation of ipratropium bromide inhaled via the breath-activated DPI is a safe and effective alternative to the chlorofluorocarbon-propelled MDI. *Key-words: chronic obstructive pulmonary disease, COPD, ipratropium bromide, metered-dose inhaler, MDI, dry-powder inhaler, DPI.* [Respir Care 2002;47(2):159–166]

Introduction

Ipratropium bromide is a quaternary ammonium anticholinergic compound chemically related to atropine. Ipratropium bromide induces bronchodilation through a selective parasympathetic blockade of the bronchial muscarinic receptors.[1] Since cholinergic tone substantially contributes to airway narrowing in patients with chronic obstructive pulmonary disease (COPD), ipratropium bromide is a main-

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stay in the management of those patients.[2] The bronchodilator action of ipratropium bromide is dose-dependent, and the recommended dose is not a definite dose but rather a range of doses, depending on the subject, the disease, and the severity of the disease. Regular use of ipratropium bromide has been associated with improvement above baseline lung function and in acute response to bronchodilator therapy after 90 days.[3] Long-term treatment with ipratropium bromide could be associated with improvement in dyspnea, especially in a subgroup of responder patients who show $\geq$ 15% increase in baseline forced expiratory volume in the first second (FEV_1) after administration of 80 μg of ipratropium bromide.[4]

Metered-dose inhalers (MDIs) have proven safe, effective, and convenient for delivering ipratropium bromide to COPD patients. However, several drawbacks encountered with MDIs have led to the development and testing of alternative devices such as dry powder inhalers (DPIs). DPIs do not require the coordination of actuation and inhalation that many patients are unable to perform with MDI.[5] Moreover, DPIs use no propellants, such as chlorofluorocarbon (CFC), which contributes to depletion of the ozone layer in the stratosphere. The Montreal Protocol, which was adopted by several governments in 1987 and has been modified 5 times to date, aims to reduce and eventually eliminate emission of man-made ozone-depleting substances.[6] In this context, DPI may be a suitable alternative for administering inhaled drugs. Recently a DPI that uses lactose as an excipient was designed for ipratropium bromide inhalation. Earlier powder inhalation formulations of ipratropium bromide used anhydrous glucose as the carrier substance, but the rate and extent of water uptake is less with lactose than with glucose, so the lactose-excipient DPI is less sensitive to environmental humidity than glucose-excipient DPI.

It is therefore important to study the efficacy of the lactose-excipient DPI and to compare its efficacy and safety profile to other established devices. The aim of the present study was to compare the safety and efficacy of ipratropium bromide in COPD patients when taken as an inhaled powder via the lactose-excipient DPI and as a pressurized aerosol via MDI. We used a cumulative dose-response model and also evaluated the tolerability and patient acceptance of the DPI.

Methods

Patients

Thirty-nine patients with clinical diagnoses of COPD (based on American Thoracic Society criteria[7]) were recruited. The study was conducted in accordance with the Helsinki declaration, as amended in Hong Kong in 1989, and the protocol was approved by the Ethics Committee of University Hospital-Lyon, Lyon, France. Written, informed consent was obtained from each patient before entry into the trial. To be eligible, a patient had to:

- Be over 40 years old
- Have a smoking history of more than 10 pack-years
- Have moderate to severe airway obstruction, with a baseline $FEV_1 < 65\%$ of predicted, an initial $FEV_1 <$ 70% of the forced vital capacity (FVC), and a $\geq$ 15% increase in FEV_1 above baseline 45 min after 80 μg (ie, 4 puffs × 20 μg/puff) of ipratropium bromide via MDI.

Exclusion criteria were: severe cardiovascular disturbance, history of cancer within the last 5 years, thoracotomy, bronchiectasis, cystic fibrosis, history of asthma, allergic rhinitis, atopy, eosinophil count above 500/mm^3, current abuse of alcohol or other drugs, and intolerance to inhaled ipratropium bromide or lactose. No patient should have experienced a respiratory infection nor have been hospitalized for an exacerbation within 6 weeks of the study. Cromolyn sodium, nedocromil, β blocker medication, and long-term oxygen therapy were not allowed throughout the trial, but inhaled corticosteroids could be used, provided that the dose remained unchanged for at least 6 weeks prior to the study and that they were continued at the same dose and taken at the same time of day throughout the trial period. Oral steroid therapy was not an exclusion criterion if daily doses were < 10 mg prednisone equivalents, provided that the patient had been on such a low-dose therapy for at least 1 year. No patient should have changed the dose of other respiratory medications during the previous 6 weeks. Other medications were withheld for appropriate periods on each study day.

Metered-Dose Inhaler and Dry Powder Inhaler

The MDI is a CFC-propelled device that delivers 20 μg ipratropium bromide per puff. The DPI is a breath-activated inhaler into which is inserted a capsule containing a nominal dose of 20 μg ipratropium bromide. After closing the inhaler, the capsule is pierced at both ends by pushing a button, and the patient inhales through the mouthpiece (Fig. 1). The studied DPI provides inhalable particles with a mass median aerodynamic diameter of 4.3 μm. The average aerodynamic particle mass < 5.8 μm is 6 μg ipratropium bromide. Because of a slight deposit into the device, the average delivered dose is 17.8 μg ipratropium bromide.

Study Protocol

We performed an open, randomized, 2-way crossover study. After a screening visit, each patient was trained to obtain a good technique when inhaling either from an MDI or a DPI and when performing pulmonary function tests. Inhalation techniques were regularly checked afterwards.

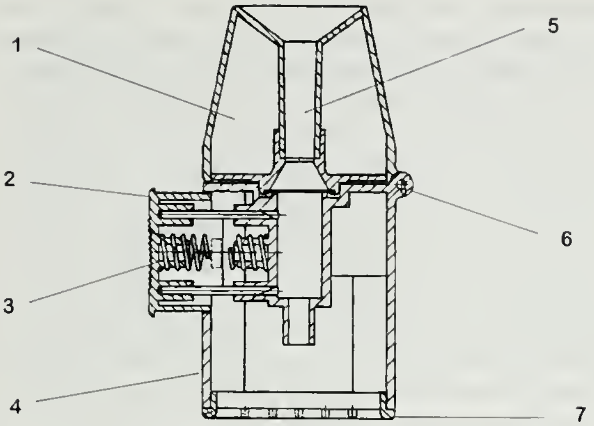

Fig. 1. The dry powder inhaler (DPI). This is a breath-activated inhaler into which a capsule containing 20 μg of ipratropium bromide is inserted. The inhaler is closed, the capsule is pierced at both ends by pushing the button, and the patient inhales through the mouthpiece. 1 = mouthpiece, 2 = piercing button, 3 = spring, 4 = base, 5 = central chamber, 6 = pin, 7 = bottom.

Clinical status was assessed by cardiopulmonary physical examination, and patients were interviewed at the beginning of each study day in order to identify patients with acute exacerbations or recent instability of clinical state.

Baseline pulmonary function tests at inclusion were always determined in the morning, and reversibility was defined as an FEV_1 increase ≥ 15% 45 ± 5 min after inhalation of 80 μg ipratropium bromide via MDI. The first study day was at least 24 h but not more than 7 d after inclusion. Pre-dose FEV_1 was measured at the same time (± 30 min) as baseline FEV_1. Then we recorded FEV_1, FVC, peak expiratory flow, pulse rate, blood pressure, and electrocardiogram (ECG). Five minutes later, the patient took 20 μg ipratropium bromide via MDI or via DPI, according to the randomization. Patients inhaled increasing doses of ipratropium bromide at 50 min intervals, until a cumulative dose of 320 μg was reached. Inhaled and cumulative doubling doses were: 20 μg and 20 μg at 0 min, 20 μg and 40 μg at 50 min, 40 μg and 80 μg at 100 min, 80 μg and 160 μg at 150 min, and 160 μg and 320 μg at 200 min. FEV_1, FVC, heart rate, and blood pressure were measured before and 45 min after each inhalation and at 15–40 min intervals up to 380 min (180 min after the last inhalation). A 45 min interval between each inhalation and pulmonary function measurement was chosen according to the delayed bronchodilator effect of ipratropium bromide and also in order to obtain a substantial accumulation of the compound.

The interval between study Days 1 and 2 was at least 48 h. Protocol requirements during Day 2 were identical to those of Day 1, except for the pre-dose FEV_1, which had to be within a range of 80–120% of the baseline FEV_1 value recorded on Day 1. Otherwise, FEV_1 stability was checked again on 2 consecutive days. If the difference was still > 20%, the patient was considered nonstable and withdrawn from the study.

Drug wash-out periods before baseline pulmonary functions tests on study Day 1 and study Day 2 were 8 h for short-acting β_2 agonists and anticholinergics, 18 h for oral β_2 agonists, 24 h for short-acting theophylline, 36 h for once-daily oral β_2 agonists, 48 h for long-acting inhaled β_2 agonists and antihistamines, and 72 h for long-acting theophyllines.

The primary outcome measure of the efficacy study was FEV_1 increase between baseline and 45 min after the last dose (195 min). Secondary outcome measures were the FVC increase between baseline and 45 min after the last dose (195 min), the FEV_1 increase at 230–380 min (determined as the area-under-the-curve for FEV_1 increase from baseline divided by the number of hours), and the FEV_1 and FVC values at each time point during each study day. End points for the safety analysis were pulse rate, systolic and diastolic blood pressure, heart rate, and corrected QT intervals measured with a 12-lead ECG performed at baseline and at 270 min.

Patient preferences were evaluated using verbal scales. At the end of Day 1 and Day 2, acceptability of the device was scored from 1 to 4 according to the following scale: 1 = very difficult to use, 2 = quite difficult to use, 3 = rather easy to use, 4 = very easy to use.

Patient preference for either day was assessed as follows: 1 = I prefer the first day of the test, 2 = I prefer the second day of the test, 3 = I have no preference between the 2 days of the test.

Patient preference for one device was assessed at the end of Day 2 by the following question: Do you think the manipulation of the dry powder inhaler is: 1 = less easy than with the metered-dose inhaler, 2 = as easy as the metered-dose inhaler, 3 = somewhat easier than the metered-dose inhaler, 4 = much easier than the metered-dose inhaler.

Statistical Analysis

Statistical analysis was performed with a commercially available software package (Statistical Analysis System, SAS Institute, Cary, North Carolina). All values are expressed as mean ± SD, except on the graphs, where mean ± SEM are presented, and statistical significance was taken as $p < 0.05$ (2-sided). A population size of 36 patients was calculated to obtain a 90% power to detect at least a 10% difference in FEV_1 variations between the 2 devices.

Results

Population and Study

The trial population consisted of 39 male patients included by the 7 centers that participated in the study. Six

Table 1. Characteristics of the Patient Population for Efficacy Analysis

	DPI-MDI (*n* = 19)	MDI-DPI (*n* = 17)
Age (y)	59.0 ± 7.3	61.8 ± 9.2
Smoking status (pack-years)	43 ± 11	35 ± 11
Concomitant respiratory therapies (*n*)		
β_2 agonists	16	14
anticholinergics	10	9
corticosteroids	6	10
theophyllines	6	10
others	9	7
Body height (cm)	167 ± 4	168 ± 7
Body weight (kg)	73 ± 12	73 ± 18
Pulse rate (beats/min)	78 ± 12	75 ± 9
Systolic blood pressure (mm Hg)	132 ± 9	134 ± 15
Diastolic blood pressure (mm Hg)	78 ± 8	78 ± 12
FVC (L)	2.18 ± 0.55	2.22 ± 0.74
FEV_1 (L)	1.03 ± 0.26	1.13 ± 0.43
FEV_1 (% of predicted)	35 ± 9	39 ± 14
FEV_1 30 min after dose	1.32 ± 0.31	1.43 ± 0.51
% FEV_1 ipratropium reversibility	29 ± 9	29 ± 13

DPI = dry powder inhaler
MDI = metered-dose inhaler
FVC = forced vital capacity
FEV_1 = forced expiratory volume in the first second
There was no difference at inclusion between the 2 sequence groups.
Except for concomitant respiratory therapies, values are mean ± SD

patients were included by 6 centers and 3 patients by the last one. The mean age was 59.8 ± 8.4 years (range 44–81 y). The mean duration of COPD was 12 ± 8 years (range 0–36 y). All patients were either active smokers (14/39) or ex-smokers (25/39) with smoking histories of > 10 pack-years (mean 39.8 ± 11.5, range 15–70). Two patients did not perform the complete pulmonary function profiles and were not included in the efficacy analysis but were included in the safety analysis. One patient decided not to participate in the study before the first study day and was not assessable for efficacy or safety analysis. Therefore 36 patients were available for the efficacy analysis and 38 patients for the safety analysis. The interval between Day 1 and Day 2 was 3.5 ± 0.6 d.

Efficacy Analysis

There was no difference between the 2 sequence groups at inclusion (Table 1). Both DPI and MDI produced significant improvement in pulmonary function. Figure 2 shows the FEV_1 cumulative dose-response curves. With both formulations, 80–90% of the bronchodilator response was obtained after the first 2 doses of 20 μg ipratropium bromide. Analysis of variance (ANOVA) showed no significant difference in treatment effect between the 2 devices in term of absolute values (p = 0.60), absolute change from baseline (p = 0.58), or relative change from baseline (p = 0.79). Table 2 shows the calculated FEV_1 area-under-the-curve values. ANOVA showed no statistically signif-

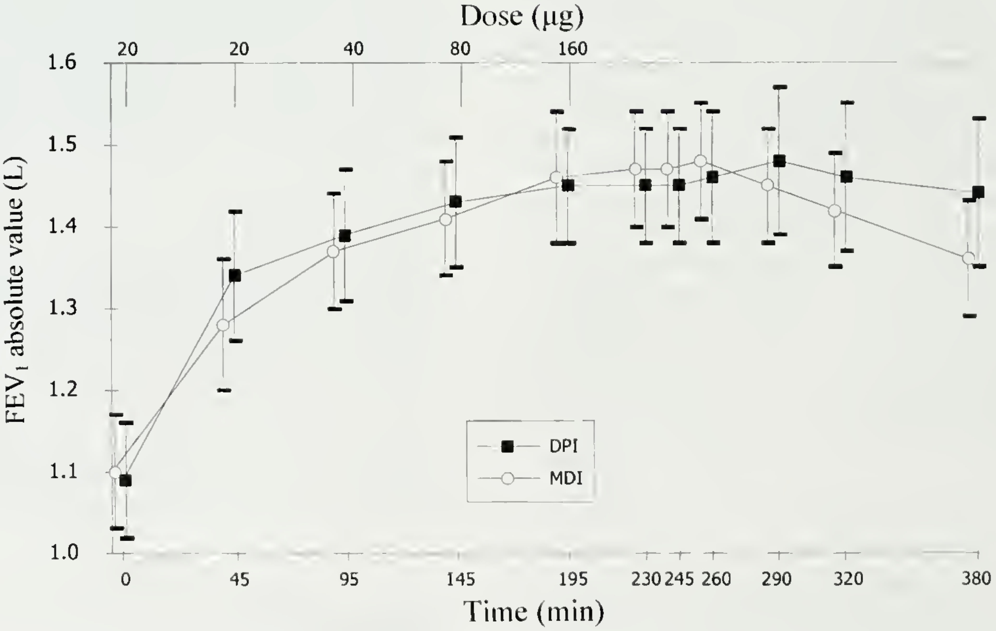

Fig. 2. Dose-response curves of forced expiratory volume in the first second (FEV_1) values. Mean FEV_1 absolute values are shown at baseline (0 min) and after increasing doses of ipratropium bromide delivered via either dry powder inhaler (DPI) or metered-dose inhaler (MDI). Values are mean ± SEM.

icant difference between the treatment groups, either from baseline to 230 min or from 230 to 380 min. Thus, persistence of response was comparable between the devices.

The cumulative dose-response curves of FVC were compared between the 2 treatment groups, and ANOVA showed no significant difference between the 2 devices for absolute values ($p = 0.15$), absolute change from baseline ($p = 0.44$), or relative change from baseline ($p = 0.47$). Figure 3 shows the absolute variations in FVC from baseline. In Table 2, area-under-the-curve values for FVC are given for the 2 parts of the dose-response curve: from baseline to 230 min during the dose-response phase, and from 230 to 380 min during the elimination phase. No significant difference was found between the 2 devices.

Table 2. Area-Under-the-Curve of FEV_1 and FVC Values*

	DPI	MDI
FEV_1 absolute values −5 to 230 min (L)	323 ± 104	318 ± 102
FEV_1 absolute values 230 to 380 min (L)	219 ± 73	213 ± 65†
FEV_1 absolute changes −5 to 230 min (mL)	65 ± 38	60 ± 39
FEV_1 absolute changes 230 to 380 min (mL)	55 ± 35	51 ± 39†
FVC absolute values −5 to 230 min (L)	615 ± 142	600 ± 153
FVC absolute values 230 to 380 min (L)	410 ± 102	402 ± 107†
FVC absolute changes −5 to 230 min (mL)	110 ± 68	100 ± 71
FVC absolute changes 230 to 380 min (mL)	88 ± 60	86 ± 81†

*$n = 36$

FEV_1 = forced expiratory volume in the first second

FVC = forced vital capacity

DPI = dry powder inhaler

MDI = metered-dose inhaler

Values are mean ± SD

†$n = 35$

Analysis of variance showed no statistically significant difference between the treatment groups, either from baseline to 230 min or from 230 to 380 min.

Safety Analysis

Six mild adverse events were observed, in 4 patients: ventricular ectopic beats on ECG with MDI at 270 min (70 min after reaching the maximum cumulative dose of 320 μg), bad taste with both MDI and DPI, and slight transient rise in blood pressure (in the same patient during each study day) with both MDI and DPI. Two moderate adverse events were observed, in 2 patients: transient ventricular ectopic beats on ECG with DPI at 270 min (70 min after reaching the maximum cumulative dose of 320 μg) and moderate bronchospasm with MDI at 200 min (just after receiving the maximum cumulative dose of 320 μg). The latter patient received treatment of 5 mg inhaled salbutamol solution and 40 mg intravenous methylprednisolone hemisuccinate, and the bronchospasm stopped after 100 min.

By ANOVA, dose-response curves for absolute values and absolute changes of pulse rate were not statistically different between the 2 groups from baseline to 380 min ($p = 0.63$ and $p = 0.13$, respectively). Furthermore, no significant dose effect was found, even until 380 min ($p = 0.35$), indicating that cumulative doses up to 320 μg of ipratropium bromide have no effect on pulse rate. Twenty-four to 48 hours after the end of the study day, mean pulse

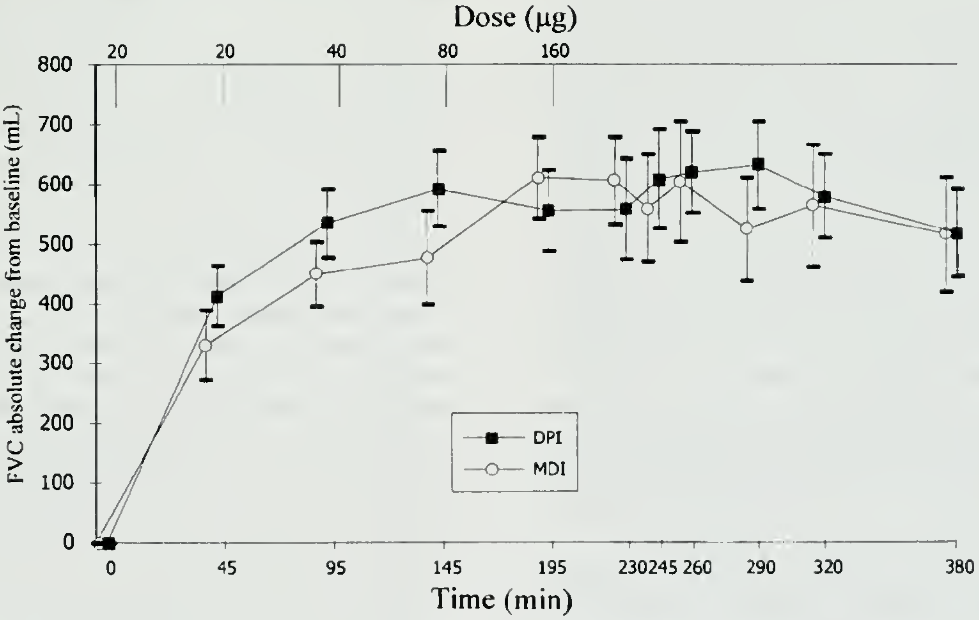

Fig. 3. Dose-response curves of forced vital capacity (FVC) changes from baseline. Mean FVC absolute changes from baseline are shown from baseline (0 min) and after increasing doses of ipratropium bromide delivered via either dry powder inhaler (DPI) or metered-dose inhaler (MDI). Results are expressed as mean ± SEM.

rate was not different between the groups (78 ± 11 beats/min with DPI vs 78 ± 12 beats/min with MDI, $p = 0.90$).

Heart rate and corrected QT interval on ECG measurements were unchanged after the cumulative dose administration, and these were similar in both groups. No interaction, sequence effect, or diurnal effect was found in this analysis.

ANOVA of absolute values and absolute changes in systolic blood pressure found no significant dose or time effect (respectively, $p = 0.94$ and $p = 0.90$ from baseline to 230 min, and, respectively, $p = 0.39$ and $p = 0.29$ until 380 min). ANOVA of absolute values and absolute changes of diastolic blood pressure found no significant dose or time effect (respectively, $p = 0.69$ and $p = 0.61$ from baseline to 230 min, and, respectively, $p = 0.58$ and $p = 0.48$ until 380 min). Twenty-four to 48 hours after the completion of the study days, diastolic and systolic blood pressures were no different between the groups.

Patient Acceptability

The handling of the DPI was considered easier than the MDI ($p = 0.014$), and the DPI was preferred to the MDI ($p < 0.001$). The patient ease-of-use scores (mean ± SD) were 3.72 ± 0.45 for the DPI and 3.31 ± 0.71 for the MDI ($p = 0.014$). The patient preference scores (mean ± SD) were 3.17 ± 0.45 for the DPI, and 2.64 ± 0.68 for the MDI ($p < 0.001$). Fifty-six percent of the patients considered the DPI easier to use than the MDI.

Discussion

The bronchodilator action of ipratropium bromide is a dose-dependent phenomenon; the recommended dose is not a *definite* dose but a *range* of doses, depending on the subject, the disease, the time, and the severity of the disease.[8] It is essential that a new device have equal or better efficacy and an equally favorable safety profile as an established device. Moreover, the results must be generated through the entire range of routinely given doses. To comply with those requirements, a comparison is needed not only of single doses but also of dose-response curves. A cumulative dose-response study is more powerful than a single-dose study to detect small bronchodilator and safety differences.[9,10] Furthermore, such a study permits a safety evaluation of multiple inhalations and accumulation of excipient. Our study was not placebo-controlled because the efficacy of ipratropium bromide had already been established for COPD patients.[11–13]

The 2-way cross-over design of our study was chosen to reduce interpatient variability of pulmonary function measurements. The doses of 20 and 320 μg correspond, respectively, to half of the recommended therapeutic dose (40 μg) and to the highest authorized dose. A 20 μg dose was used to investigate the initial part of the dose-response curve. A 45 min interval was chosen between each inhalation and pulmonary function measurement in relation to the interval to the peak of bronchodilation of ipratropium bromide and also in order to obtain a substantial accumulation of the compound. A double-blind design was not considered appropriate to evaluate the safety profile of different excipients in 2 different formulations. Safety would not be adequately proven by the administration of standard doses, but rather by gradually increasing doses.[14] Cumulative doses are a convenient means to produce more bronchodilation than a single equivalent dose[9] and are considered a proper means to estimate efficacy and safety of inhaled bronchodilators[10] in real-life situations such as an "as-required" basis or repeated inhalations during an acute exacerbation. One of the advantages of the cumulative dose-response design is that the response can be followed across a wide dose range. Moreover, a dose-response curve allows good discrimination of 2 different inhaled formulations delivering different inhaled doses.[15]

A potential bias in the interpretation of our study could be that we used a fully open-labeled design. However, blinding the patients to treatments would have been extremely difficult, since the MDI and DPI devices could not be made identical. A double-dummy design would have solved that problem, but has a serious drawback: such a design would have lead to the administration of excipients of both formulations, which would have made interpreting inhalation-related adverse events almost impossible. Thus, the study was open-labeled. In such a study of different devices, blinding the study personnel is a possible option, but would be difficult to implement in 7 centers, since the pulmonary function tests at baseline and after dosing would have to be conducted separately from the administration of the drug, by another technician, in a different room. Few centers would be able to comply with such a protocol because of inadequate staffing (or even areas) dedicated to the study.

Our study shows a large and identical improvement in pulmonary function values with ipratropium bromide delivered via DPI or MDI. With both devices the most important bronchodilating effect is obtained with the lowest doses—about 20% and 30% increase in FEV_1 with cumulative doses of 20 and 40 μg, respectively. The subsequent additional doses did not markedly improve pulmonary function, since the curves reached a plateau level with the highest cumulative doses (about 40% with FEV_1). These results were confirmed by the comparability of pulmonary function area-under-the-curve values measured from 230 to 380 min (elimination part of the curve) as well as from baseline to 230 min (dose-response curve) for both absolute values and variations from baseline. The comparison of area-under-the-curve values covering the period after the last inhalation also shows a similar post-dose profile for the 2 formulations. Those results are consistent with previous studies comparing a glucose-excipient powder formulation to the pressurized aerosol of ipratropium bromide in patients with COPD[16,17] or asthma.[18,19] In a population of COPD patients with acute reversibility after inhalation of bronchodilators, Gross et al performed a cumulative dose-response study using ipratropium bromide via nebulization.[11] They used 5 doses from 50–600 μg of nebulized ipratropium bromide and found that the optimal dose in patients with stable COPD is about 400 μg via nebulizer, which is equivalent to 160 μg via MDI. Thus, Gross et al found a similar optimal ipratropium bromide dose to our study, with both MDI and DPI. Moreover, as in our study, they did not observe any adverse effects at any ipratropium bromide dose.

Our results indicate that large doses of inhaled ipratropium bromide (up to 320 μg) have no clinically relevant effect on pulse rate or blood pressure. This is consistent with the remarkably good tolerability and lack of systemic effects of inhaled ipratropium bromide reported in the literature.[20] The rate and type of adverse events were similar for both devices. The number of reported adverse events was low, and no severe adverse effects were described. Only one local adverse effect was reported: a bad taste at the end of each study day. One moderate adverse event with MDI was a bronchospasm that required therapy, but which was due to the interruption of other pulmonary medications before the study day. Thus, we conclude that ipratropium bromide has a comparable safety profile when administered via MDI or DPI. Furthermore, the evaluation of handling and acceptability indicates that the DPI was considered easier to use than MDI and was more acceptable to our study population.

Active patient participation is necessary to obtain an adequate inhalation technique with MDI. Most patients and some medical staff[21] do not acquire satisfactory MDI technique. In addition, MDI is not adapted to elderly or pediatric patients with poor coordination.[5] Thus, the development of alternative inhaled pharmaceutical forms is important.[22–24] Dry powder formulations of bronchodilator drugs should be considered a satisfactory alternative to MDI. DPIs are CFC-free and thus safe for the environment, and they are breath-activated and therefore do not require hand-mouth coordination. The DPI device appears to be easier to use and more practical than a conventional MDI and is at least as well tolerated. Such advantages may greatly improve patient compliance.

Conclusions

This study indicates that cumulative doses (20–320 μg) of a lactose-excipient form of ipratropium bromide have efficacy and safety profiles similar to a marketed MDI form of ipratropium bromide among COPD patients. Hence, ipratropium bromide in a lactose excipient delivered via DPI is a satisfactory and safe alternative to the conventional CFC-propelled MDI.

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Churg-Strauss Syndrome Occurring 30 Years After the Onset of Ulcerative Colitis

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Aikaterini Ch Pantelidaki MD PhD, and Charis S Roussos MD PhD

Churg-Strauss syndrome (CSS) is a rare pulmonary and systemic vasculitis associated with asthma, with peripheral blood and/or tissue eosinophilia. We report the case of a 53-year-old woman who was admitted to the hospital with pneumonia and coma secondary to right hemisphere intracerebral hemorrhage. Although she recovered from the pneumonia, she remained comatose and had sinusitis and persisting blood eosinophilia. A muscle biopsy revealed eosinophilic vasculitis. The diagnosis of CSS was made and the patient recovered after being treated with prednisone and cyclophosphamide. This case reports the very rare appearance of CSS 30 years after the first appearance of ulcerative colitis and 27 years after the onset of asthma. *Key words: Churg-Strauss syndrome, CSS, ulcerative colitis, asthma, systemic vasculitis.* [Respir Care 2002;47(2):167–170]

Introduction

Churg-Strauss syndrome (CSS) is a rare disease that represents 2.2% of all vasculitis cases.[1] CSS is characterized by asthma, peripheral blood and/or tissue eosinophilia, and evidence of systemic vasculitis.[1,2] CSS appears to emerge with a highly variable delay after the onset of asthma,[2,3] and it has rarely been described in association with ulcerative colitis or other inflammatory bowel diseases.[4–6] We report the case of a 53-year-old woman with longstanding ulcerative colitis, asthma, allergic rhinitis, sinusitis, peripheral eosinophilia (> 1,500 cells/mL), central nervous system involvement, and eosinophilic vasculitis on muscle biopsy, and who developed CSS 30 years after the first appearance of ulcerative colitis.

Case Summary

A 53-year-old woman was admitted to the intensive care unit (ICU) with coma and acute respiratory failure requiring intubation and mechanical ventilation.

The patient had a history of allergic rhinitis for 35 years and of asthma for 27 years. Treatment for asthma included inhaled bronchodilators (salmeterol), oral theophylline, and inhaled corticosteroids; she had been treated for 5 years with an oral corticosteroid, which had been discontinued 2 years prior to admission. The patient had never taken leukotriene-modifying agents.

Thirty years prior to admission the patient had been diagnosed with ulcerative colitis on the basis of symptoms and the findings of 2 large-bowel biopsies performed in a German hospital. She had been in clinical remission for the last 3 years under treatment with mesalazine.

One year prior to admission the patient had an acute myocardial infarction. No coronary arteriogram was performed.

Ten months prior to entry she experienced weakness, myalgias, and mild fatigue. White blood count showed peripheral eosinophilia (14%, 1,572 cells/mL). All her symptoms improved with acetaminophen. A new laboratory examination was not performed.

Seven months prior to admission she was hospitalized at another hospital with coma and right hemiparesis, which were diagnosed as a stroke and which resolved completely

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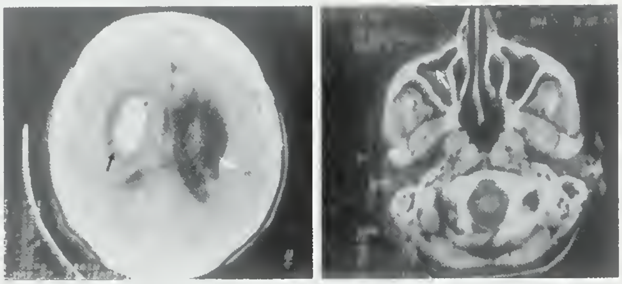

Fig. 1. Cranial computed tomograms. Left: Large intracerebral hemorrhage and mild edema in the right basal ganglia, with no midline shift (black arrow), and old ischemia injury in the left basal ganglia area, with no traction of the lateral ventricle (white arrow). Right: Air-fluid level and inflammatory elements (white arrow) in right maxillary sinus.

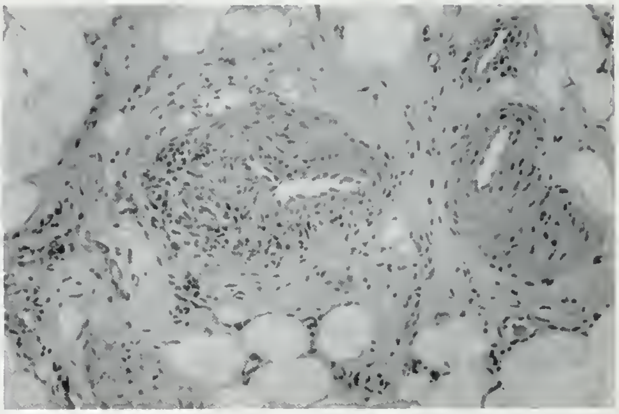

Fig. 2. Muscle biopsy shows wall thickening of small vessels, lumen stenosis, and predominantly eosinophilic inflammatory infiltration of the vessel walls (H-E × 100).

over the next 2 months. She had never been checked for systemic disease.

On the morning of ICU admission, the patient presented with loss of consciousness and cyanosis. She was intubated, set on mechanical ventilation, and transferred to the ICU. Physical examination on ICU admission showed body temperature 39° C, blood pressure 100/60 mm Hg, and heart rate 110 beats/min. She had left hemiplegia, and auscultation revealed crackles throughout both lungs. There was no evidence of malignancy.

Laboratory findings included hematocrit 33%, leukocyte count 23,400 cells/mL (43% eosinophils), and platelets 313,000 cells/mL. All other laboratory tests were normal. Urine findings showed no hematuria, proteinuria, or casts. A chest radiograph showed diffuse interstitial and alveolar infiltrates in both lungs. Bronchoalveolar lavage showed $> 10^5$ colony-forming units/mL of *Pseudomonas aeruginosa*, which was also recovered in blood culture.

Computed tomography showed a right-sided intracerebral hemorrhage, mild edema in the right basal ganglia, evidence of old ischemic infarct in the left basal ganglia, and evidence of inflammation elements in the paranasal sinuses (Fig. 1).

The patient was treated with ceftazidime and amikacin. Mesalazine was discontinued. Her condition gradually improved and the chest radiograph infiltrates resolved. She was weaned from ventilatory support and extubated on hospital day 24, but remained comatose and had persistent severe eosinophilia (4,000–20,000 eosinophils/mL). No viral, fungal, or parasitic disease was discovered. C-reactive protein was 17 mg/dL (normal value < 0.5 mg/dL), rheumatoid factor was 280 international units/mL (normal value < 20 international units/mL), and serum immunoglobin E (IgE) was 682 mg/dL (normal value < 100 mg/dL). Both perinuclear antineutrophil antibodies and cytoplasmic antineutrophil antibodies were negative. A bone marrow analysis showed increasing cellularity and a marked increase of megakaryocytes, which in some areas were forming rolls. Erythrocytes were rare, whereas the eosinophils were substantially increased, with a few myelocytes present. No blasts were observed. Overall, the bone marrow findings were compatible with primary or secondary hypereosinophilic syndrome. A trapezoid muscle biopsy showed wall thickening of small vessels, lumen stenosis, and predominantly eosinophilic inflammatory infiltration of the vessel walls, indicative of a late eosinophilic vasculitis (Fig. 2).

The diagnosis of CSS was made and the patient was treated daily with intravenous methylprednisone (1 mg/kg/d) plus monthly intravenous cyclophosphamide (0.6 g/m^2 body surface area). The patient was discharged from the ICU on day 45, exhibiting only central nervous system-related abnormalities (she was lethargic and had left hemiparesis). Three months after hospital discharge she had 700 eosinophils/mL and the above-mentioned neurologic deficit.

Discussion

CSS is a rare disorder, with an annual incidence of 2.4 per million.[7] CSS is characterized by eosinophilia and small-vessel vasculitis (ie, it affects arteries but has a predilection for smaller vessels).[8] CSS occurs in individuals with asthma and allergic rhinitis,[1,2] whereas it has been rarely described in association with ulcerative colitis and other inflammatory bowel diseases.[4–6]

In our patient, the CSS diagnosis was based on the presence of at least 4 of the CSS criteria (according to the traditional format classification defined[9] by the American College of Rheumatology): longstanding asthma, severe eosinophilia (> 1,500 cells/mL) for at least 6 months, radiographic opacification of the paranasal sinuses, and vasculitis with intra- and extra-vascular eosinophils in the trapezoid muscle biopsy. The lack of extra-vascular granulomas in our patient may be explained by the fact that the aforementioned CSS-associated pathologies are all concurrently present in life only in a minority of patients.[10]

Patients with inflammatory bowel disease, especially ulcerative colitis, can develop a variety of respiratory problems, including pulmonary infiltrates with eosinophilia,[5] cutaneous[5] and pulmonary vasculitis,[4] and drug-related pulmonary or systemic toxicity (mesalazine, sulfasalazine).[5] Although there is no way to prove the link between the ulcerative colitis and the CSS in our patient, there are several other anecdotal cases in the literature in which ulcerative colitis preceded the onset of CSS,[4,6] which supports our hypothesis. Could the bowel inflammation have been eosinophilic? The diagnosis of ulcerative colitis was made 30 years ago in Germany after 2 large-bowel biopsies; evidence of eosinophilic enteritis was not reported and should be excluded.

The delay between the first appearance of ulcerative colitis and CSS in this patient is probably the longest reported, and could be explained by:

1. CSS is characterized by 3 phases: prodromal, secondary, and life-threatening vasculitic phase.[11] Our patient might have been in the first or second CSS phase for all those years, and CSS onset was probably due to disease advancing despite standard therapies.

2. Our patient was on oral steroids for a long time, and their discontinuation 2 years prior to admission may have contributed to the late appearance of eosinophilia and CSS.

Mesalazine administration should not be the cause of CSS, since it may induce eosinophilic lung disease, systemic lupus erythematosus, hepatitis, and nephritis, but not vasculitis.[5] In addition, the discontinuation of the drug did not reduce the eosinophilia, making the diagnosis of mesalazine toxicity unlikely.

Though asthma is a central feature of CSS (> 90%), Lanham et al reported that there is occasional remission of asthma with the onset of vasculitis, and 58% of patients were free of asthma in the early stages of their vasculitic disease.[11] This is most likely the case with our patient. Another interesting point in our report is the very long delay of CSS appearance, as compared to the onset of asthma. To our knowledge, this 27-year delay is the longest ever reported. In most reported cases, systemic vasculitis emerges with a mean delay of 3 years in patients who subsequently die,[2,3] and with a delay of 13 years in survivors.[3] Eosinophilia usually coexists with the onset of vasculitis[11] but it may also appear well before the vasculitic event,[11] as in the present case.

Pulmonary infections are not unusual in CSS patients.[11] In the Hammersmith Hospital cases, Lanham et al reported an incidence of more than 40% of recurrent pulmonary infections in CSS patients.[11] However, severe lung infections requiring ICU admission, as in our patient, are rare, and death due to respiratory failure is reported in only 2% of the cases.[11] In our patient the lung infiltrates might have been eosinophilic, but they resolved after antibiotic therapy and prior to the administration of steroids, so they should be attributed to pulmonary infection.

The old myocardial infarction and the episodes of cerebral hemorrhage in this patient could be due to CSS-related coronary-vessel[10] and cerebral vasculitis,[12] respectively. However, no coronary angiogram had been performed, so there is no way to prove the aforementioned speculation. Nevertheless, in our patient 5 pathologies coexisted—ulcerative colitis, asthma, CSS, acute myocardial infarction, and stroke—that could all be part of a single disease process, although their causal connection remains uncertain.

In CSS, glucocorticoid therapy alone or in association with cyclophosphamide or plasmapheresis is beneficial, with a 7-year survival rate of 72–83%.[13] CSS patients with one or more of the following have poorer prognosis than those without: proteinuria > 1 g/d, renal insufficiency (serum creatinine > 1.58 mg/dL), gastrointestinal tract involvement, cardiomyopathy, or central nervous system involvement.[14] These patients should receive more intensive treatment with cytotoxic drugs.[14] Since our patient had developed central nervous system involvement, she was treated with a high dose of cyclophosphamide (bolus of 0.6 g/m^2 body surface area per month) and prednisone (1 mg/kg/d).[14]

Conclusions

Systemic vasculitis has been reported to coexist with both asthma and inflammatory bowel disease. This case reports:

1. The very rare delayed appearance of CSS after the first manifestation of ulcerative colitis, and

2. The coexistence of ulcerative colitis, asthma, CSS, acute myocardial infarction, and stroke, which might all be part of a single disease process.

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Practical Management of Acute Asthma in Adults

Teal S Hallstrand MD MPH and John V Fahy MD

Introduction
Epidemiology
Pathogenesis
Clinical Assessment
Acid-Base Issues and Hypoxemia
β Adrenergic Agonists
Anticholinergics
Corticosteroids
Methylxanthines
Leukotriene Modifiers
Magnesium Sulfate
Assessment of the Response to Therapy
Heliox
Noninvasive Ventilation
Mechanical Ventilation
General Anesthesia
Follow-Up
Summary

All asthma patients are at risk for acute asthma exacerbations. Moderate to severe exacerbations account for many emergency department visits and subsequent hospitalizations each year. Recent studies have advanced our understanding of the pathogenesis and treatment of acute asthma. The purpose of this review is to provide practical guidance in the assessment and treatment of adults with acute asthma in the hospital setting. Managing patients with acute asthma involves assessing the severity of the exacerbation, implementing measures to rapidly reverse airflow limitation, and instituting therapies that limit the progression of airway inflammation. Some patients may benefit from other supportive measures such as heliox and noninvasive ventilation. If the patient continues to deteriorate and requires mechanical ventilation, then ventilator settings that minimize the risk of hyperinflation should be chosen. After an episode of acute asthma, long-term preventive medications, especially inhaled corticosteroids, should be prescribed and education should be provided to prevent future episodes. *Key words: asthma, status asthmaticus, acute severe asthma, β adrenergic agonist, anticholinergic, leukotriene, corticosteroid, mechanical ventilation, heliox, noninvasive ventilation.* [Respir Care 2002;47(2):171–182]

Introduction

Asthma exacerbations account for over 1.8 million emergency department visits each year in the United States.[1] Recent advances in our understanding of the pathogenesis of asthma and studies evaluating the effectiveness of therapies for acute asthma have led to improvements in acute asthma management. During the evaluation of a patient

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with acute asthma, the clinician should be able to assess the severity of the exacerbation, implement measures that will rapidly reverse airflow obstruction, and initiate anti-inflammatory therapy that will prevent the progression of airflow limitation and prevent relapse of the exacerbation. The purpose of this review is to provide practical guidance for the assessment and treatment of adults with acute asthma in the emergency department and hospital settings. This is not meant to be an all-inclusive review of the literature on acute asthma, but rather it is meant to highlight information likely to prove useful to the clinician making decisions regarding the management of an individual patient. The evidence provided in this review is based on studies of the pathophysiology of acute asthma and on clinical trials evaluating the efficacy of therapeutic interventions.

Epidemiology

Over the past decade, asthma prevalence has risen steadily in the United States, and there are now over 14 million individuals with asthma.[1] All of these individuals are at risk for the development of acute asthma. Patients with mild asthma are clearly at risk for severe asthma exacerbations. For example, in a series of patients who died of severe asthma, 13% of adults and 23% of children had asthma characterized as mild prior to the fatal exacerbation (Table 1).[2,3] Patients with the highest risk of developing severe asthma exacerbations are those who have experienced prior severe asthma episodes, especially within the previous year.[4–6] Among patients requiring mechanical ventilation for severe asthma, common precipitants include upper respiratory infection (61%), which is usually viral, exposure to smoke or allergen (13%), poor compliance with prescribed asthma medications (12%), and comorbid substance abuse.[7] In inner-city populations as many as a third of patients who die of asthma are substance abusers.[8] Severe asthma exacerbations occur in individuals of all ethnicity and socioeconomic status.[7] In some individuals who suffer near-fatal asthma there is evidence of diminished perception of dyspnea.[9] Poor compliance with therapy and delays in seeking medical attention are frequently noted in individuals who die of asthma.[2,3] Accelerated use of bronchodilators identifies patients who are at risk for severe asthma exacerbations: the risk of fatal or near-fatal asthma is significantly higher among patients using > 1.4 canisters (20,000 μg) of albuterol per month.[10] A pattern of increasing use of bronchodilators is associated with the greatest risk of a severe asthma exacerbation.[11] Early recognition of an impending asthma exacerbation is of foremost importance in the management of the asthmatic patient and stresses the vital role of education in the management of all levels of asthma severity.

Table 1. Distribution of Asthma Severity Prior to a Fatal Asthma Exacerbation

Prior Severity	Adults (%)	Children (%)
Mild	13	23
Moderate	22	41
Severe	65	36

(Adapted from References 2 and 3.)

Pathogenesis

Airway inflammation is a common feature of asthma, even in patients with mild asthma.[12] Specifically, there is an inflammatory cell infiltrate composed of activated T lymphocytes (ie, Th2 and Tc2 cells), eosinophils, and degranulated mast cells.[13,14] In addition, structural changes occur that may or may not be a consequence of airway inflammation. These structural changes are collectively referred to as airway remodeling and include goblet cell hyperplasia, subepithelial collagen deposition, smooth muscle hypertrophy and hyperplasia, submucosal gland enlargement, and bronchial microvascular enlargement and proliferation. In contrast to the findings in chronic asthma, autopsy studies of airway inflammation in patients who die suddenly of acute asthma have revealed more neutrophils than eosinophils. This is especially so in the airways of patients with rapidly progressive respiratory failure from severe asthma.[15] Clinical studies have also revealed prominent neutrophilic airway inflammation and increased production of mucin-like glycoprotein in patients presenting to the hospital with severe asthma (Fig. 1).[16–18] This points to the possibility that there are 2 distinct variants of acute asthma. Patients who show a slow progressive course over days to weeks may have prominent allergic inflammation with eosinophils in the airways, whereas patients who present abruptly have more neutrophils in their airways and more mucus plugging, possibly caused by viral infection. This theory may lead to the development of specific therapies to decrease neutrophil recruitment to the airways in acute severe asthma.

Clinical Assessment

Every patient entering the emergency department with a suspected asthma exacerbation should be assessed promptly with a focused history and physical examination to identify the process as an asthma exacerbation and to determine the level of severity. Moderate acute asthma is characterized by dyspnea while talking, increased respiratory rate and pulse rate, and use of accessory muscles of respiration. Moderate acute asthma is generally associated with a peak expiratory flow (PEF) of 50–80% of predicted

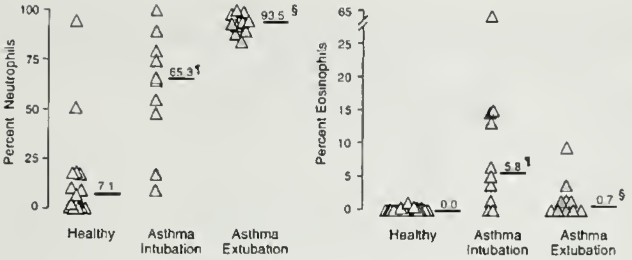

Fig. 1. Percentage of neutrophils (left panel) and eosinophils (right panel) in tracheal aspirates from patients with acute severe asthma requiring mechanical ventilation and a control group of patients intubated for nonpulmonary surgery (Healthy). Airway secretions were obtained within 12 h of intubation (Asthma Intubation) and within 12 h of extubation (Asthma Extubation). (From Reference 16, with permission.)

or of personal best.[19] Patients with acute severe asthma can often be identified clinically by the typical upright posture and use of accessory respiratory muscles, indicating that substantial energy is devoted to the work of breathing (WOB). Patients may be anxious, scared, and unable to talk in full sentences. The medical history should not delay the initiation of therapy and should determine the rate of progression of the exacerbation, recent medical therapy, and prior episodes of respiratory failure, and should exclude alternative diagnoses such as upper airway obstruction and congestive heart failure. The physical examination should focus on assessing the severity of the exacerbation, excluding upper airway obstruction, and identifying complications of acute asthma. Physical signs that occur during acute severe asthma include an upright posture, diaphoresis, sternocleidomastoid retraction, respiratory rate > 30 breaths/min, pulse > 120 beats/min, and pulsus paradoxus > 12 mm Hg (Table 2),[20] although when a patient fatigues these physical signs may no longer be present and are therefore not as reliable. Wheezing correlates poorly with the degree of airflow obstruction and often wheezing becomes louder as airflow is restored.[21]

Possible complications of severe asthma include pneumomediastinum, pneumothorax, subcutaneous emphysema, mucus plugging, and atelectasis. Air in the soft tissues and in the pericardial space can be identified on physical examination. Unilateral absence of breath sounds should alert the clinician to the possibility of pneumothorax or mucus plugging with resultant atelectasis or lobar collapse. Upper airway obstruction can masquerade as asthma and should be excluded early in the evaluation. Stridor, drooling, and swollen tongue and lips may suggest upper airway obstruction. Chest and neck radiographs should be obtained in selected patients to exclude upper airway obstruction or mechanical complications, or when there is a history suggestive of pneumonia. PEF measurement may be of some value initially, but is of most value in determining the response to therapy. Spirometry and PEF maneuvers should be used cautiously in patients who have features of severe airflow obstruction, because of the bronchoconstrictor effect of a deep inspiration on inflamed airways in asthma.[22] PEF < 50% of predicted or < 120–200 L/min indicates a severe exacerbation.[19] In patients with severe asthma, an initial arterial blood gas measurement is indicated to detect hypercapnia and to assess the degree of hypoxemia. Generally, patients with hypercapnia have PEF < 30% of predicted on presentation.[23]

Table 2. Physical Findings During Acute Severe Asthma

Upright Posture
Diaphoresis
Sternocleidomastoid retraction
Respiratory rate > 30 breaths/min
Heart rate > 120 beats/min
Pulsus paradoxus > 12 mm Hg
Peak expiratory flow < 30–50% of predicted or < 120–200 L/min

Acid-Base Issues and Hypoxemia

Oxygen saturation should be assessed via pulse oximetry on all patients being evaluated for acute asthma. Mild hypoxemia that is easily corrected with low-dose oxygen therapy (eg, 2–4 L/min via nasal canula) is generally present in individuals with acute asthma. Hypoxemia is easily corrected with oxygen because the etiology is a mismatch between air and blood flow, created by regional differences in airflow (ie, ventilation-perfusion mismatch).[24] High-dose oxygen administration may be a factor in the development of hypercapnia and should be used with caution.[25] Hypoxemia that is not easily corrected should lead to a search for an alternative diagnosis or for complications such as lobar collapse, pneumothorax, or pneumonia. Arterial blood gas measurement often reveals respiratory alkalosis initially, but patients may develop respiratory acidosis if their respiratory muscles fatigue. A compensatory nonanion-gap metabolic acidosis is frequently present when the exacerbation is days in duration. An anion-gap metabolic acidosis develops in some patients, probably representing lactic acidosis.[26]

β Adrenergic Agonists

The most effective and safest choice of initial therapy to relieve airflow obstruction in a patient presenting with acute asthma is a selective β_2 adrenergic receptor agonist given via inhalation. The selective β_2 agonists in clinical use today have an onset of action of approximately 5 min and a duration of action of 3–6 h. The dose of β_2 agonist necessary to relieve airflow obstruction depends on the

Table 3. Continuous Versus Intermittent Albuterol Nebulization for Acute Severe Asthma

	All Patients		PEF < 200 L/min		p
	Continuous	Intermittent	Continuous	Intermittent	
n	47	52	35	34	—
PEF (L/min) at 0 min	163	183	135	137	NS
PEF (L/min) at 60 min	256	248	239	202	< 0.05
PEF (L/min) at 120 min	310	291	296	244	< 0.05
Heart rate (beats/min) at 120 min	83	101	90	104	< 0.05

PEF = peak expiratory flow
NS = not significant
(Adapted from Reference 36.)

severity of airway inflammation, the amount of β_2 agonist used prior to reaching the hospital, and the delivery device used. Patients who use a lot of inhaled β_2 agonist prior to presenting to the hospital may have a reduced response to β_2 agonist therapy, because of a decrease in β_2 adrenergic receptor sensitivity. This reduced sensitivity can be overcome by administering higher doses of β_2 agonist[27] and by administering systemic corticosteroids.[28] Because the dose-response relationship for β_2 agonists is log-linear, a 10-fold increase in the dose of β_2 agonist is necessary to achieve a 1-fold increase in clinical response.[29] In adults who are not responding to lower doses of a β_2 agonist, intermittent doses of 2.5–5.0 mg of albuterol may be given via nebulizer every 20 min or via continuous nebulization of a total dose of 10–15 mg over 1 h.[19] Patients should be carefully monitored for adverse effects from β_2 agonists, including arrhythmia, tachycardia, tremor, hypotension, hypokalemia, hyperglycemia, and hypomagnesemia.

Recent studies have shown that in many instances delivery of β_2 agonist can be readily accomplished via metered-dose inhaler (MDI) with holding chamber (ie, spacer) rather than via nebulizer.[30–34] For example, in moderate acute asthma, equal efficacy was found for four 100 μg doses of inhaled albuterol via MDI every 30 min or 2.5 mg of nebulized albuterol every 30 min.[32] The total amount of albuterol administered via MDI with holding chamber is substantially less than that delivered via nebulizer and is therefore associated with fewer adverse effects.[30] However, studies evaluating the efficacy of the MDI holding chamber as a delivery system for β_2 agonists in acute severe asthma have included only limited numbers of patients with severe airflow obstruction (eg, forced expiratory volume in the first second [FEV_1] $\leq$ 30% of predicted or PEF $\leq$ 120 L/min); therefore, nebulizer is preferred if the exacerbation is severe or if there is any concern about the patient's ability to cooperate with the treatment. When using a nebulizer, continuous nebulization is more effective than intermittent administration in patients with severe airflow obstruction and may reduce adverse effects (Table 3).[35,36] Continuous nebulization can be administered to patients with refractory asthma until the episode

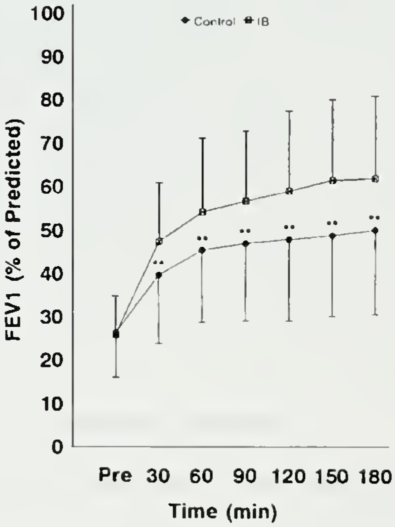

Fig. 2. Comparison of forced expiratory volume in the first second (FEV_1 percent of predicted) in patients with acute severe asthma randomized to either albuterol (Control: lower curve) or albuterol plus ipratropium bromide (IB: upper curve). Data points are mean values, and brackets represent 1 standard deviation. The double-asterisks (**) indicate $p < 0.01$. (From Reference 42, with permission.)

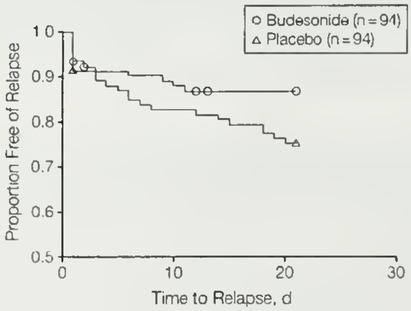

Fig. 3. Kaplan-Meier relapse curves from patients treated with inhaled budesonide or placebo in addition to a 7-day course of prednisone following emergency department treatment for acute asthma. (From Reference 54, with permission.)

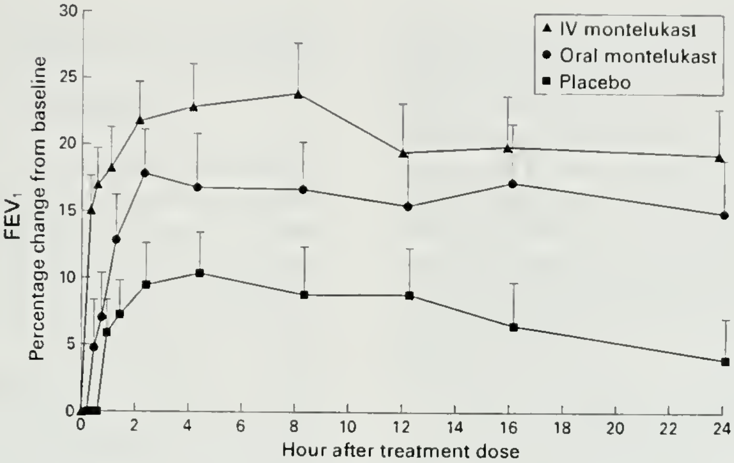

Fig. 4. The effect of intravenous (IV) montelukast (7 mg), oral montelukast (10 mg), and placebo on forced expiratory volume in the first second (FEV$_1$ percentage change from baseline) in patients with persistent asthma. (From Reference 65, with permission.)

resolves. Intravenous and subcutaneous β_2 agonists should generally be avoided in all but the most severe exacerbations, because they may worsen hypoxemia, are associated with more adverse effects and may play a role in the development of lactic acidosis.[37,38] There may be a role for subcutaneous β_2 agonists in patients with the most severe asthma, in whom delivery of inhalational agents to the lower airways may be compromised. For example, subcutaneous administration of epinephrine improved PEF in 60% of patients not responding to 2 h of inhaled metaproteronol.[39] Epinephrine should be used cautiously if at all in pregnant women, because of vasoconstriction of uteroplacental blood flow.

Anticholinergics

The autonomic nervous system plays a regulatory role in the tone of normal and asthmatic airways. Stimulation of these parasympathetic fibers through the vagus nerve leads to smooth muscle contraction and mucus release. Although parasympathetic activity plays only a minor role in the pathogenesis of chronic asthma, it may substantially contribute to airflow obstruction in acute severe asthma. Anticholinergic agents used in the management of asthma block parasympathetic activity by antagonizing the muscarinic cholinergic receptors. Tertiary ammonium compounds such as atropine are easily absorbed from the gastrointestinal tract and cross the blood brain barrier, leading to substantial adverse effects. The newer quaternary ammonium compounds ipratropium bromide and glycopyrolate minimize those adverse effects because they do not cross the blood brain barrier and have minimal gastrointestinal absorption.[40]

The addition of an anticholinergic agent during treatment of acute asthma provides more effective bronchodilation than a selective β_2 agonist alone.[41] In adults, ipratropium bromide plus albuterol (480 μg albuterol and 84 μg ipratropium bromide via MDI with spacer every 10 min) resulted in a 48.1% greater improvement in FEV$_1$ at the end of 3 h of treatment than the control group that received albuterol but no ipratropium bromide (Fig. 2).[42] That finding is consistent with 2 other randomized controlled trials in adults, both of which found a modest benefit to FEV$_1$: 91 and 113 mL, respectively, higher than treatment with albuterol alone.[43,44] A meta-analysis of studies adding ipratropium to albuterol in adults concluded that the greatest benefit was in patients with the most severe airflow obstruction.[41] One study evaluated the duration of therapy and found that continued benefit is achieved by the addition of ipratropium bromide up to the first 36 h of hospitalization.[45] A decrease in hospital admission rates has been observed in a number of controlled studies.[43,46,47] Length of hospital stay was also shorter (5.4 d vs 4.1 d) for patients treated with the addition of ipratropium bromide during initial management.[45]

Corticosteroids

At present, systemic corticosteroids are the most reliable way to gain control of airway inflammation in patients with acute asthma. Systemic corticosteroids reverse the down-regulation of β_2 adrenergic receptors that occurs in patients using increased doses of β_2 agonists.[28] Most patients benefit from early institution of systemic corticosteroids during acute exacerbations. Meta-analyses of randomized controlled trials found significantly lower risk of hospital admission when systemic corticosteroids were administered.[48,49] For example, in a randomized controlled trial comparing intravenous methylprednisolone to placebo, 9 of 48 patients required hospitalization in the corticosteroid group, whereas 23 of 49 patients required admission in the control group.[50] Oral and intravenous administration appear to be equally effective, as long as the patient is able to tolerate oral medications.[49] A minimum dose of 30 mg prednisone or equivalent every 6 h initially appears to be required for good efficacy.[49] Some studies have shown a small additional benefit from doses as high as 120 mg methylprednisolone every 6 h,[51] although the magnitude is small and a number of studies do not support that more aggressive dosing regimen.[52] Oral steroids should generally be continued until PEF is $\geq$ 70% of predicted or of personal best.

After an acute exacerbation, 12–16% of patients will relapse and develop recurrent exacerbations. Oral corticosteroids clearly reduce the rate of relapse in the first 7–10 d following moderate to severe acute asthma episodes.[53] Inhaled corticosteroids should be initiated at the same time as systemic corticosteroids to prevent future asthma exacerbations, and may further reduce the relapse rate after an exacerbation. A randomized controlled trial found a 48% lower rate of relapse (defined as unscheduled office visits or worsening asthma symptoms over the first 21 d) when inhaled budesonide (1,600 μg/d) was added to a course of oral corticosteroids following an asthma exacerbation (Fig. 3).[54]

Methylxanthines

Aminophylline is relatively ineffective as a bronchodilator in patients presenting with acute severe asthma. The bronchodilating effect of aminophylline is inferior to the effect of a selective β_2 agonist,[55] and there are greater adverse effects of tremor, nausea, anxiety, and palpitations when using the combination of a β_2 agonist and aminophylline.[56] Unlike ipratropium bromide, the addition of aminophylline does not generally result in additional bronchodilation.[55] A number of studies have found that aminophylline is ineffective at improving airflow obstruction when patients are already being treated with a selective β_2 agonist.[57] However, aminophylline, like other phosphodiesterase inhibitors, has anti-inflammatory properties.[58] Despite no additional reduction in airflow limitation, some studies have noted a lower hospital admission rate with the use of aminophylline.[59,60] For example, in a placebo-controlled trial of low-dose aminophylline (mean concentration 9.7 mg/L), although airflow obstruction was no different with the addition of aminophylline early on during therapy, there was a 3-fold difference in the admission rate: 21% in the placebo group versus 6% in the aminophylline group.[59] Other studies conflict with those findings, but a meta-analysis of 6 trials found a trend ($p = 0.06$) toward fewer hospital admissions with the addition of aminophylline.[57] A sensible approach may be to add aminophylline for a target serum concentration of 10 mg/L in patients with poor initial response to β_2 agonists, anticholinergics, and corticosteroids over a period of hours.

Leukotriene Modifiers

Leukotriene modifiers have become an important component of therapy for chronic asthma. The release of cysteinyl leukotrienes into the airways of asthmatic individuals causes smooth muscle contraction, vascular permeability, and mucus release that is mediated through a specific receptor ($CysLT_1$).[61] Cysteinyl leukotrienes also have a role in the recruitment of eosinophils to the airways. There are currently no published clinical trials using these agents in the management of acute asthma; however, it is clear that leukotrienes are released during an asthma exacerbation[62] and, therefore, blockade of leukotrienes during an asthma exacerbation may prove useful in addition to other therapies. Treatment with systemic corticosteroids does little initially to suppress the release of leukotrienes during acute asthma,[63] indicating that blockade of leukotrienes could complement the role of corticosteroids in managing airway inflammation during acute asthma. In patients with moderate stable asthma, an oral dose of zafirlukast has a bronchodilating effect that occurs within an hour and that is additive to the effect of β_2 agonist.[64] Intravenous montelukast, which is not yet available clinically, causes bronchodilation within 15 min that is sustained for 24 h in patients with mild to moderate stable asthma (Fig. 4).[65] In a pilot phase II study in which 201 patients with acute asthma were randomized to intravenous montelukast or placebo in addition to standard care, there was a significant ($p < 0.01$) additive improvement in FEV_1 at 20, 40, and 60 min after montelukast infusion, amounting to approximately 140 mL greater improvement in FEV_1 at the 20 min measurement point.[66] Further research is necessary to determine if leukotriene blockade during acute asthma has a beneficial role as an additive bronchodilator and anti-inflammatory therapy that complements the role of corticosteroids.

Magnesium Sulfate

Hypomagnesemia may be present in patients with severe asthma, especially after prolonged use of β_2 agonists. Magnesium sulfate inhibits smooth muscle contraction through an effect on calcium channels. In case series, intravenous infusion of magnesium sulfate resulted in significant bronchodilation in patients with severe asthma, although less than with albuterol.[67,68] Studies on the use of magnesium sulfate in acute asthma have shown that it is a safe and well tolerated addition to other acute asthma therapies. Adding magnesium sulfate to other treatments for a moderate asthma exacerbation has no significant effect on measures of expiratory flow or hospital admission rate.[69–71]

However, patients with the most severe airflow obstruction, usually with failure to initially respond to albuterol, appear to benefit from the addition of magnesium sulfate.[69-72] In a meta-analysis that included pediatric studies, Rowe et al found an overall 9.8% improvement in FEV_1 (percent of predicted) and a significantly lower hospital admission rate among patients with acute severe asthma treated with magnesium sulfate.[73] It is reasonable to add magnesium sulfate to other therapies for acute severe asthma in adults, at a dose of 1–2 g over 20–40 min in patients without renal disease.

Assessment of the Response to Therapy

Patients who are improving with therapy should ideally be observed for 6 h to determine the likelihood of relapse.[19] Patients who attain a stable PEF of $> 70\%$ of predicted or of their prior best are generally safe to discharge with close follow-up (Fig. 5). Patients with incomplete response to therapy, generally with PEF in the range of 50–70% of predicted, should be admitted to a general medical ward equipped for frequent respiratory treatments. Patients with PEF $< 50\%$ of predicted, hypercapnia, altered sensorium, or deterioration in the emergency department should be admitted to the intensive care unit.

Heliox

Increased WOB in patients with severe asthma results in part from turbulent airflow across narrowed airways. Heliox (a blend of helium and oxygen, usually given as a 70:30 mixture) is less dense than air and crosses narrowed airways with less resistance. This decreases the WOB and may reduce fatigue in patients with severe asthma. In a randomized controlled trial of 23 patients with acute severe asthma, PEF was improved by 58.4% after 20 min of heliox, compared to a 30% oxygen placebo (Fig. 6).[74] The effect of heliox ceases immediately on discontinuing the mixture and has no long-term effect on airflow limitation. In some patients who are not deteriorating rapidly but are fatiguing, heliox may be considered in an attempt to reduce the WOB as a "bridge" to avoid the need for mechanical ventilation. The ability of heliox to avoid the need for mechanical ventilation has not been determined. During mechanical ventilation, heliox decreases P_{aCO_2} and peak airway pressure and therefore may protect against barotrauma.[75] The use of heliox during mechanical ventilation also may facilitate reducing the fraction of inspired oxygen.[76]

Noninvasive Ventilation

Noninvasive positive-pressure mask ventilation may decrease WOB in asthma patients, but there are no controlled trials evaluating this as a supportive therapy for asthma. In an uncontrolled series of 21 patients with acute severe asthma, nasal continuous positive airway pressure of 5–7.5 cm H_2O improved dyspnea scores and reduced respiratory rates.[77] In another series of 17 patients with acute severe asthma, noninvasive positive-pressure ventilation using an inspiratory pressure averaging 14 cm H_2O and an expiratory pressure of 4 cm H_2O reduced hypercapnia and improved hypoxemia.[78] Noninvasive ventilation should not be a substitute for intubation in a patient who is deteriorating, who has a decreased level of consciousness, or who has increased airway secretions.

Mechanical Ventilation

Patients who are deteriorating and becoming progressively fatigued should be intubated to gain better airway control and provide ventilatory support. The decision to intubate is primarily a clinical judgment. Patients with respiratory arrest, circulatory collapse, or intractable respiratory acidosis should clearly be placed on mechanical ventilation. Other signs that may reflect the need for mechanical ventilation include altered level of consciousness, increasing respiratory muscle fatigue, inability to talk in full sentences, and rapid deterioration despite aggressive treatment measures. Hypercapnia is only a relative indication for mechanical ventilation. In a series of patients presenting with hypercapnia, only 5 of 61 patients required mechanical ventilation.[79]

Once the decision to institute mechanical ventilation has been made, it is important to select a ventilator mode and settings that minimize hyperinflation. Lung hyperinflation results in decreased venous return to the right ventricle and can cause hypotension and death. In particular, high minute ventilation, in the period immediately following intubation or subsequently, is to be avoided. There should be no impetus to quickly normalize P_{aCO_2}; rather, the goal should be to maintain adequate oxygenation and pH ≥ 7.2. Although there have been no direct comparisons to assess different ventilator strategies for acute severe asthma, it has been found that mortality rates were lower in studies that used a strategy of permissive hypercapnia once mechanical ventilation was initiated (Table 4).[80] Because relatively low minute ventilation may be difficult to tolerate for the patient with acute severe asthma, it is necessary to administer adequate sedation, and it may even be necessary to administer neuromuscular blocking agents, but only when the patient continues to have difficulty interacting with the ventilator despite treatment with drug combinations that include high doses of benzodiazepines, narcotics, or propofol. The use of neuromuscular blocking agents in managing acute severe asthma is associated with a risk of prolonged neuromuscular weakness following discontinuation of treatment.[81]

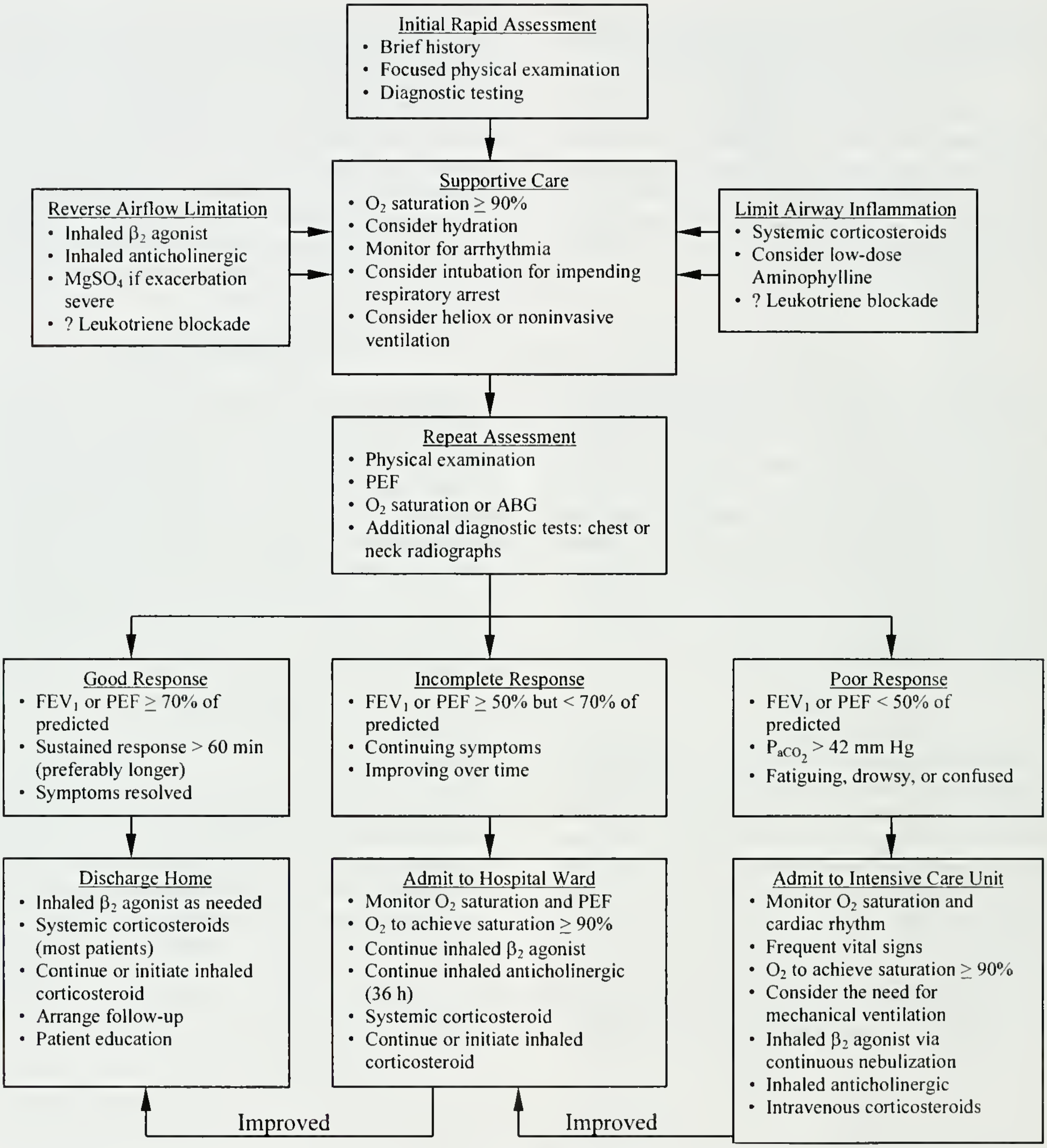
Initial Rapid Assessment
• Brief history
• Focused physical examination
• Diagnostic testing
Reverse Airflow Limitation
• Inhaled β_2 agonist
• Inhaled anticholinergic
• $MgSO_4$ if exacerbation severe
• ? Leukotriene blockade
Supportive Care
• O_2 saturation $\geq 90\%$
• Consider hydration
• Monitor for arrhythmia
• Consider intubation for impending respiratory arrest
• Consider heliox or noninvasive ventilation
Limit Airway Inflammation
• Systemic corticosteroids
• Consider low-dose Aminophylline
• ? Leukotriene blockade
Repeat Assessment
• Physical examination
• PEF
• O_2 saturation or ABG
• Additional diagnostic tests: chest or neck radiographs
Good Response
• FEV_1 or PEF $\geq 70\%$ of predicted
• Sustained response > 60 min (preferably longer)
• Symptoms resolved
Incomplete Response
• FEV_1 or PEF $\geq 50\%$ but $< 70\%$ of predicted
• Continuing symptoms
• Improving over time
Poor Response
• FEV_1 or PEF $< 50\%$ of predicted
• $P_{aCO_2} > 42$ mm Hg
• Fatiguing, drowsy, or confused
Discharge Home
• Inhaled β_2 agonist as needed
• Systemic corticosteroids (most patients)
• Continue or initiate inhaled corticosteroid
• Arrange follow-up
• Patient education
Admit to Hospital Ward
• Monitor O_2 saturation and PEF
• O_2 to achieve saturation $\geq 90\%$
• Continue inhaled β_2 agonist
• Continue inhaled anticholinergic (36 h)
• Systemic corticosteroid
• Continue or initiate inhaled corticosteroid
Admit to Intensive Care Unit
• Monitor O_2 saturation and cardiac rhythm
• Frequent vital signs
• O_2 to achieve saturation $\geq 90\%$
• Consider the need for mechanical ventilation
• Inhaled β_2 agonist via continuous nebulization
• Inhaled anticholinergic
• Intravenous corticosteroids
Improved
Improved

Fig. 5. Overview of the initial management and disposition of patients treated for acute severe asthma. PEF = peak expiratory flow. ABG = arterial blood gas measurement. FEV_1 = forced expiratory volume in the first second.

High peak airway pressure, which is usually present during a severe asthma exacerbation, reflects high airway resistance from bronchoconstriction. Increased peak pressures should be treated aggressively with bronchodilators and anti-inflammatory therapies and may additionally be reduced by the use of heliox (see above).[75] High plateau pressures (eg, > 30 cm H_2O) are often present, resulting from air trapping and hyperinflation rather than a decrease in static lung compliance. Air trapping occurs because the expiratory time is prolonged by bronchoconstriction and is insufficient to permit full exhalation to occur prior to the initiation of the next breath, resulting in elevated intrinsic

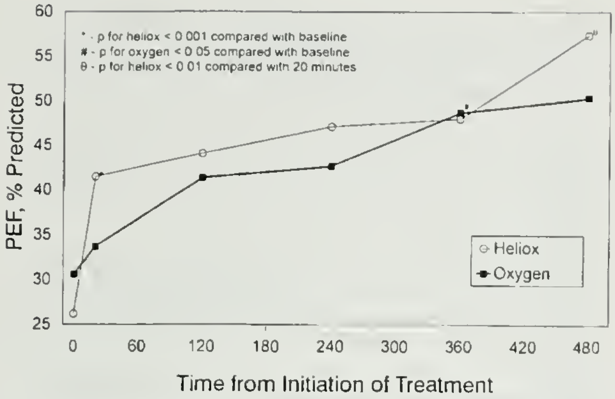

Fig. 6. The effect of heliox (70% helium, 30% oxygen) on peak expiratory flow (PEF percent of predicted) in individuals with acute severe asthma, compared to a control group who received 30% oxygen. (From Reference 74, with permission.)

positive end-expiratory pressure (auto-PEEP). Air trapping increases the risk of barotrauma and results in decreased venous return that may necessitate volume loading with intravenous crystalloid solutions. Air trapping can be minimized by measures that prolong the expiratory time, including reducing respiratory rate (and therefore minute ventilation) and increasing inspiratory flow (eg, ≥ 100 L/min). Other measures that decrease the minute ventilation by limiting carbon dioxide production include deep sedation or paralysis and avoidance of overfeeding.

General Anesthesia

The inhalational anesthetic diethyl ether was noted long ago to cause bronchodilation. Halothane, enflurane, and isoflurane are inhalational anesthetics in current use that have similar bronchodilatory properties. In 12 patients treated with 1% halothane during acute severe asthma requiring mechanical ventilation there was a rapid reduction in airflow obstruction, improvement in peak airway pressure, and reduction in hypercapnia.[82] Inhalational anesthesia should only be used as a measure of last resort, since prolonged use is associated with substantial risks, including arrhythmia, myocardial depression, and vasodilation leading to hypotension.

Follow-Up

A severe asthma exacerbation, especially a near-fatal event, should prompt close follow-up to prevent further severe asthma episodes and to lessen the risk of fatal asthma. In the year following an asthma hospitalization, the relative risk of subsequent hospitalization for asthma is 16 times as great as for an asthmatic not hospitalized in the prior year.[4] The risk of a fatal asthma exacerbation in the 6 years following intensive care unit admission for asthma is 22.6% for all ages, 36.2% in adults over the age of 40, and especially high in cigarette smokers.[83]

Education for patients suffering severe asthma exacerbations should include a strong message about the need to regularly use controller medications, especially an inhaled corticosteroid, to prevent asthma exacerbations, and a clear action plan to identify an impending exacerbation so that additional therapy can be added promptly. In this group of patients, monitoring PEF at home may be useful to detect the onset of an exacerbation and to monitor the effect of therapy.[19] Patients with a history of severe asthma may be poor perceivers of the severity of airflow obstruction,[9] and a change in PEF may help those individuals recognize an impending exacerbation. Additionally, elevated PEF variability, representing incomplete suppression of airway inflammation, is a substantial risk factor for hospitalization

Table 4. Comparison of Available Case Series Using Either Permissive Hypercapnia or Traditional Mechanical Ventilation During Treatment of Acute Severe Asthma

Year Published	With Permissive Hypercapnia						Without Permissive Hypercapnia			
	1984	1990	1991	1992	1992	1994	1983	1986	1986	1992
Number in series	34	24	59	61	73	35	26	34	48	32
Mortality rate (%)	0	0	3.4	3.3	4.0	3	23	9	2*	22
Days on MV†	2.5	NA	0.7	2	NA	1.5	NA	4.9	1.6	3.6
Complications (*n*)										
Barotrauma	3	3	3	1	17	3	3	6	1	6
Hypotension	15	NA	16	NA	27	4	NA	12	17	8
Pneumonia	7	2	5	2	NA	NA	1	12	NA	8
Arrhythmia	4	3	14	7	8	0	NA	NA	NA	7

*29 of 48 episodes represent a single patient

†Mean number of days of mechanical ventilation (MV)

NA = not available

(Adapted from Reference 80.)

for asthma.[4,6] Poor compliance with therapy has been noted in individuals who suffer fatal asthma exacerbations;[2] therefore, in patients with a history of near-fatal asthma, every effort should be made to provide education about the need for ongoing preventive therapy

Summary

Acute asthma can occur in all asthma patients, although the highest risk is with patients who have had prior episodes of life-threatening asthma. Rapid recognition and early intervention with anti-inflammatory therapies, primarily corticosteroids, prevents the progression of the exacerbation. Bronchodilation and relief of airflow obstruction is best achieved with a selective inhaled β_2 agonist along with an anticholinergic agent. Magnesium sulfate should be considered if there is severe airflow obstruction or poor initial response to β_2 agonists. Aminophylline and leukotriene modifiers may prove useful for acute asthma, when used in addition to other therapies, although additional research on this subject is required. Patients with delayed response to therapy but who are not deteriorating rapidly may benefit from heliox or noninvasive ventilation to gain time to allow anti-inflammatory therapies to take effect. If mechanical ventilation is required, a strategy that minimizes the risk of hyperinflation and hemodynamic instability should be employed. The patient should be admitted to the hospital unless there is rapid clinical resolution and restoration of PEF to > 70% of predicted. When the patient is discharged from the hospital a clear plan should be in place to effectively treat airway inflammation, and the patient should be carefully educated about asthma and the means to prevent further episodes of acute asthma.

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Detection of Patient-Ventilator Asynchrony During Low Tidal Volume Ventilation, Using Ventilator Waveform Graphics

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Introduction

A 55-year-old woman with pneumonia and septic shock developed acute respiratory distress syndrome (ARDS) and was enrolled into the low tidal volume (V_T) ventilation study of the National Heart, Lung, and Blood Institute's ARDS Network.[1] The protocol required that V_T be reduced to as low as 4 mL/kg (predicted body weight) to minimize ventilator-induced lung injury by maintaining the end-inspiratory plateau pressure (P_{PLAT}) $\leq$ 30 cm H_2O. (For further information on the ARDS Network protocol, go to the ARDS Network web site at http://hedwig.mgh.harvard.edu/ardsnet/.) The patient's breathing was supported with a mechanical ventilator (Dräger E-1, Dräger, Telford, Pennsylvania) in the volume assist/control mode. On ARDS Day 2, the patient required positive end-expiratory pressure (PEEP) of 16 cm H_2O and fraction of inspired oxygen (F_{IO_2}) of 0.90 to maintain P_{aO_2} of 70 mm Hg. V_T of 290 mL (4.9 mL/kg) and respiratory rate of 32 breaths/min were required to keep $P_{PLAT} \leq 30$ cm H_2O and produce pH of 7.33 and P_{aCO_2} of 47 mm Hg. Trigger sensitivity was set at –1 cm H_2O below PEEP, and peak inspiratory flow was set at 80 L/min. During periods of controlled mechanical ventilation when spontaneous breathing attempts were absent, intrinsic PEEP measurements were consistently 1 cm H_2O above the set PEEP level. Clinicians noted intermittent periods when the measured P_{PLAT} varied between 24 and 40 cm H_2O, whereas the exhaled V_T often fluctuated by > 100 mL (or 1.7 mL/kg). During these periods, spontaneous breathing attempts were noted and the total respiratory rate was seldom more than 4 breaths above the set respiratory rate. On physical examination the patient appeared to be asynchronous with the ventilator. Her inspiratory efforts appeared to commence at peak inspiration, and intermittently she was able to trigger extra mechanical breaths. Coincidentally, an esophageal balloon had been placed to calculate transmural central venous pressure, and a pulmonary mechanics monitor (Ventrak, Novametrix, Wallingford, Connecticut) attached to the esophageal balloon assessed patient-ventilator interactions (Fig. 1).

Questions

1. Using the negative deflections in esophageal pressure (P_{ES}) to locate the patient's inspiratory effort, are there corresponding abnormalities in the appearance of the flow, airway pressure (P_{AW}), and V_T scalar waveforms?

2. Based on the appearance of the flow, P_{AW}, and V_T scalar waveforms, can inspiratory efforts that successfully triggered mechanical breaths be distinguished from those that failed to trigger extra breaths?

3. Based on the difference between the end-expiratory P_{ES} and the P_{ES} at the point where inspiratory flow and P_{AW} become positive, can the intrinsic PEEP level be estimated?

Answers

In Figure 1, Point A represents a "noncaptured" inspiratory effort in which the patient could not trigger a breath from the ventilator. The noncaptured breathing effort can be detected by 3 aspects of the expiratory waveforms. First, there was a premature drop in expiratory flow, to 0 L/min, followed by an additional phase of expiratory flow. Second, early in the expiratory phase there was a sharp drop in P_{AW} to PEEP, followed by the P_{AW} transiently rising back above PEEP at the end of the second expiratory phase. Furthermore, in all ventilator-delivered breaths that were followed by a premature inspiratory effort, there was no stable P_{PLAT}, only a steady downward pressure-

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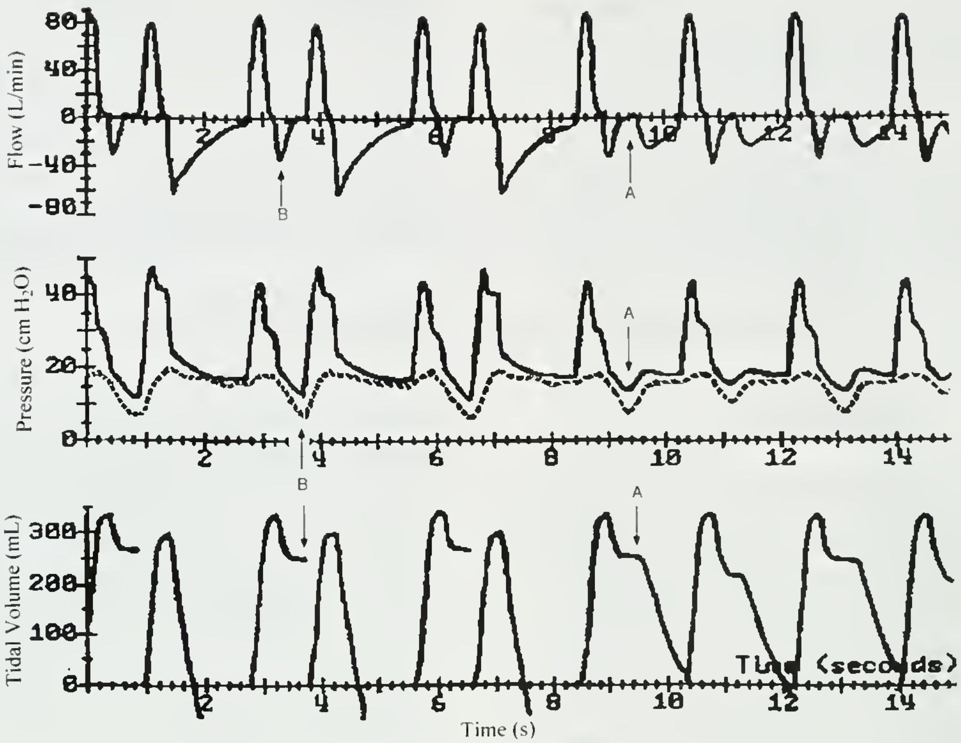

Fig. 1. Scalar tracings of flow (top), airway pressure (middle, solid curve), esophageal pressure (middle, dashed curve), and tidal volume (lower) exhibiting evidence of patient-ventilator asynchrony during lung-protective ventilation.

slope that paralleled the deflection in P_{ES}. Third, the suspension of expiration caused by the noncaptured inspiratory effort resulted in a plateau during the expiratory decay in the V_T waveform. Point B represents a patient breathing effort sufficiently strong to trigger the ventilator into inspiration, resulting in a "stacked" breath. This also is noted by 3 features in the waveforms. First, there was an abrupt drop in expiratory pressure below PEEP, followed by an inspiratory phase in which both the peak P_{AW} and the P_{PLAT} were elevated above the preceding controlled breath. This suggested that the end-inspiratory volume and pressure had exceeded the target level for lung protection. Second, the inspiratory effort caused an early disruption in expiratory flow, with an apparently diminished peak expiratory flow. (However, as all breaths in this tracing either have a truncated expiratory flow pattern because of patient effort or an augmented peak expiratory flow as the trapped volume is expelled from the lungs from an elevated driving pressure, it is not possible to determine what the patient's peak expiratory flow would have been in the absence of breathing effort.) Third, there was an abrupt truncation in the expiratory volume tracing after the plateau. On the subsequent volume waveform, the expiratory volume fell below 0 mL, indicating at least partial exhalation of the volume trapped during the previous breath.

On the breath preceding Point B that was captured by the ventilator's trigger system, end-expiratory P_{ES} was approximately 15 cm H_2O, and the P_{ES} nadir at Point B (just preceding the positive change in flow and P_{AW}) was approximately 7 cm H_2O. Therefore, a P_{ES} change of approximately 8 cm H_2O was required to trigger a ventilator breath. Since the trigger sensitivity was set at –1 cm H_2O, the intrinsic PEEP was approximately 7 cm H_2O. On the noncaptured breathing effort (Point A), the estimated P_{ES} change was approximately 7 cm H_2O.

Discussion

When V_T was increased to 6.0 mL/kg, the patient quickly ceased all breathing effort and P_{PLAT} stabilized at 33 cm H_2O. The appearance and cessation of the patient's breathing effort was reproducible as the V_T was adjusted back and forth between 5 and 6.0 mL/kg over several minutes. The level of sedation was increased until the patient ceased all spontaneous breathing efforts. V_T was returned to 5 mL/kg to maintain $P_{PLAT} \leq 30$ cm H_2O. Because the patient's oxygenation status was precarious, we did not attempt to measure her spontaneous V_T demand to confirm patient-ventilator V_T mismatching. Alternatively, the asynchrony may be explained, in part, by a "deflation" or "gasp reflex" that is believed to aid inflation during progressive lung collapse.[2] However, 3 aspects of this case suggest that V_T mismatching was a likely source of her asynchrony:

1. The abrupt appearance and cessation of inspiratory efforts with a change in V_T.
2. The peak inspiratory flow was high, the trigger sensitivity was low, and neither variable changed with the appearance and resolution of asynchrony.
3. Patient effort occurred consistently after the delivery of V_T.

Two important points issue from this incident of patient-ventilator asynchrony. First, apparent patient-ventilator V_T mismatching may result in asynchrony, despite appropriate settings of peak inspiratory flow, mandatory respiratory rate, and trigger sensitivity. Lung-protective ventilation requires control of the end-inspiratory volume and pressure in order to prevent ventilator-induced lung injury from regional lung over-distention.[3] This case illustrates that excessive end-inspiratory lung volume and pressure paradoxically can occur when patient-ventilator asynchrony results in breath-stacking. Second, this patient's breathing efforts occurred at end-inspiration, when her lung volume and alveolar pressure were elevated. Therefore it was more difficult for her to achieve the trigger sensitivity threshold in the ventilator circuit and trigger extra breaths. Mechanically this phenomenon is similar to the "wasted efforts" that typically occur in patients with obstructive lung disease and intrinsic PEEP.[4] The esophageal pressure deflections during these uncaptured inspiratory efforts (approximately 7 cm H_2O) were similar to the effort level expended during patient-triggered breaths in ARDS when a traditional V_T size is used.[5]

In this case, the clinical importance of an elevated P_{PLAT} might not have been properly elucidated without the aid of graphics analysis. In other words, a plausible explanation for the elevated P_{PLAT} (based on the physical exam) could be transmitted intra-abdominal pressure from expiratory muscle recruitment during asynchrony. The graphics analysis ruled out that interpretation because no airway pressure "spike" appeared during the end-inspiratory pause time. In fact, P_{AW} progressively dissipated during the end-inspiratory pause time on asynchronous breaths. Furthermore, graphics analysis may facilitate detection of this problem when anasarca or abdominal distention obscures the detection of patient effort and asynchrony by physical exam.

Lung-protective ventilation requires strict control over end-inspiratory lung volumes and pressures.[3] Therefore, the liberal use of sedation and the possible addition of neuromuscular blocking agents are recommended first to treat asynchrony and dyspnea.[3] However, in some situations increasing sedation or using neuromuscular blocking agents must be avoided. Under those circumstances asynchrony can be treated either with airway pressure-release ventilation[6] or any other pressure-targeted mode that allows "free-breathing" throughout the ventilatory cycle. Although volume and pressure targets would be violated, the risk of ventilator-induced lung injury probably would be less than allowing breath-stacking to continue in a volume-targeted mode.

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Books, Films, Tapes, & Software

Reviews of Books and Other Media. Note to publishers: Send review copies of books, films, tapes, and software to RESPIRATORY CARE, 600 Ninth Avenue, Suite 702, Seattle WA 98104.

Nunn's Applied Respiratory Physiology. 5th edition. Andrew B Lumb MB BS. Foreword by JF Nunn MD DSc PhD. Oxford, United Kingdom: Butterworth Heinemann. 2000. Hard cover, illustrated, 687 pages, $115.

Although this is the fifth edition of this textbook, it is the first written by Dr Lumb. The book was initially conceived and written by Dr Nunn—a classic book that bridged basic pulmonary physiology and its clinical application. Eventually the 2 sections were separated, although the material remained integrated. The current edition takes the concept one step further by including a section on the physiology of pulmonary diseases. Though this is a textbook, I particularly liked that each chapter can be used stand-alone, given a minimal amount of basic knowledge. Furthermore, the book can be read at different levels: a first-year student can read a section to glimpse an overview, whereas the more advanced pulmonary care professional can ponder the importance of the well-crafted sentences. Thus, it becomes an invaluable reference as well as a textbook. The reader could be overwhelmed by the size of the tome (nearly 700 pages), but it is truly 3 books in one. In addition, each chapter is divided and subdivided into small sections, so that the reading can be paced and the understanding broken down into manageable portions.

The first part is entitled "Basic Principles," and it covers the usual physiology of the pulmonary system. The very first chapter, however, is unique to this book: it's about the atmosphere. Written by Dr Nunn, the chapter explains the evolution of the atmosphere, especially the oxygen and carbon dioxide in it. Though this chapter may not be crucial to understanding pulmonary physiology, it is fascinating reading. The first part also includes 1 chapter on functional anatomy, 3 chapters on the various aspects of lung mechanics, 1 on control of breathing, 1 on the pulmonary circulation, 4 on the various aspects of gas exchange, and 1 on the nonrespiratory functions of the lung. I like the way the topics are developed logically. The chapter on the control of breathing, for example, is sandwiched between the one on respiratory system resistance and the one on pulmonary ventilation, thus stressing that the muscles have to overcome the system's resistance in order for ventilation to occur, but are, in turn, controlled by respiratory neurons. The last chapter of this part is on the nonrespiratory function of the lung, and it is a nice introduction to this complex topic, even though it may become outdated sooner than the rest of the book.

Each chapter is well illustrated with diagrams, tables, and pictures, well placed and complete. Studying the figures alone, each with its detailed legend, could provide an understanding of the topics. The clinical importance of the material is always evident. For example, in discussing the diaphragm, 3-dimensional computed tomograms show a normal subject and a patient with chronic obstructive lung disease and hyperinflation, clearly showing the flattened diaphragm domes. Not only does this provide information about the disease process, it also serves to clarify the function of the diaphragm in general, since the change is dramatic and obvious even to a novice. References are provided for each chapter, and they are up to date, considering the amount of time required to write such a large book: with a copyright date of 2000, citations as late as 1998 were used.

There are several topics that normally don't appear in pulmonary physiology books, reminding us that this is truly an applied text. For example, toward the end of the chapter discussing the physiology of carbon dioxide exchange there is a section on capnography, which explains the normal capnograph tracing and what can be learned from both a normal and an abnormal capnograph—for example, the placing of a tracheal tube.

The second part of the book is on applied physiology. Some of the topics discussed here, for example exercise and altitude, appear in most basic pulmonary physiology textbooks, sometimes as separate chapters, other times together as respiratory function under stress. Other topics, for example sleep and anesthesia, are seldom found. The other chapters discuss pregnancy and lung growth, high pressure, closed environments, drowning, air pollution, anesthesia, hypocapnia and hypercapnia, hypoxia, anemia, and hyperoxia.

There are abundant clinical applications in every chapter. For example, the chapter on pregnancy, neonates, and children provides values for lung function during the 3 trimesters of pregnancy and discusses treatment of infant respiratory distress syndrome and theories of sudden infant death syndrome. The chapter on anesthesia discusses lung function during the postoperative period. The chapter on anemia provides an interesting discussion on what are the appropriate hemoglobin levels in various clinical circumstances.

The physiology of low oxygen is discussed in 2 chapters: one on high altitude and flying covers the usual material as well as information on cabin pressure and air quality. The other chapter, entitled "Hypoxia," concentrates on the cellular effects of hypoxemia, but not its causes, in contrast to the chapter on changes in carbon dioxide tension, which discusses both the causes and effects of hypocapnia and hypercapnia.

On my wish list for this part is a chapter on pulmonary function testing. Though this topic is discussed throughout the book, I would like to see the information collected together in one place, because I think it is an important clinical subject for respiratory therapists at all levels.

The third part of the book, "Physiology of Pulmonary Diseases," comprises 8 chapters. Some topics, such as artificial ventilation and extrapulmonary gas exchange, covered in one chapter each, are not diseases at all. Nevertheless, these chapters provide good discussions of the management and pathophysiologic consequences of these modalities. The chapter on lung transplantation discusses fairly recent (1998) information on indications, outcomes, and important physiologic differences between a normal lung and a transplanted one, which has no nerves or lymphatics and is exposed to immunosuppressive therapy.

Part 3 opens with a chapter on ventilatory failure, which picks up where the chapter on hypoxia left off. The remaining chapters in this part discuss pulmonary diseases, grouped in a somewhat nonstandard way, at least for an American reader. The chapter on airways diseases includes cystic fibrosis in addition to asthma and chronic obstructive pulmonary diseases. The chapter on parenchymal lung disease covers pulmonary collapse, pneumonia, and fibrosis. The pulmonary vascular disease chapter follows the norm more closely, including edema, embolism, and pulmonary hypertension. All of those chapters, and one on acute lung injury, discuss the causes, mechanisms, etiology, treatment, and measurements of the various diseases and syndromes as appropriate or known. They provide a good overview for the beginning clinician and a good source of references for further reading.

Six appendixes conclude the book. Appendix A has a very clear and detailed explanation of the international system of units (Système Internationale), which is based on the meter, kilogram, and second. The Système Internationale units are used throughout the book, alongside the older system (centimeters, grams, seconds): for example, kPa (kilopascals) along with mm Hg. Thus, this appendix is very useful. Appendixes B through D cover material that is sometimes found within the text of pulmonary physiology texts, including gas laws, conversion factors, and symbols and abbreviations. Appendix E has nomograms and correction charts, probably not as useful as they once were, given the prevalence of pocket computers. Appendix F is my favorite: a clear, succinct, and well-illustrated explanation of the mathematical functions that govern pulmonary physiology. This topic is seldom covered in a basic physiology textbook, but is so important in understanding the relationships among the variables. Many pulmonary care providers have only a fuzzy notion of the mathematics involved, so Appendix F is an excellent addition to this textbook.

This book should be on the shelf of all pulmonary professionals, from medical to respiratory care students, from respiratory physiologists to seasoned clinicians. It is a great textbook for a respiratory physiology course because the clinical correlations reinforce the basic material.

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Structure & Function of the Body, 11th edition. Gary A Thibodeau PhD and Kevin T Patton PhD. St Louis: Mosby. 2000. Soft cover, illustrated, 528 pages plus glossary and index, plus CD-ROM and companion Student Survival Guide, $32.95.

This is the 11th edition of this general anatomy and physiology text. That fact is a testimony to its continued use in curricula for the allied medical professions and nursing, including those who will become readers of RESPIRATORY CARE. It also says something positive about the book's ability to adapt to changing audiences who now expect the "textbook" to provide contemporary learning techniques such as multimedia support and web-connected learning.

The text is quite readable at the undergraduate level. It centers on 2 underlying themes: presenting normal structure and function and showing how they support homeostasis in the body. These themes are presented in the introductory chapter and followed throughout the book. The contents follow a traditional system-by-system approach that makes the book adaptable to most survey courses that would lead to more intensive study later on. Also, like most works on broad topics, it takes a modular approach to learning, with learning objectives stated at the beginning of each chapter (module) and learning evaluations at the end. The book's 330 color illustrations are generally large, bright, and clearly labeled, without being overly obtrusive in the text. There are learning boxes throughout that contain subject-related applications on health and well-being, clinical interventions, and research, issues, and trends. These are usually well-placed in the chapters and offer the kinds of applications that make anatomy and physiology more enticing to future health practitioners than would be a more mundane collection of diagrams of anatomical structures and descriptions of complex principles. As one example, in the chapter on the respiratory system there is an overview of the current National Emphysema Treatment Trial study on lung-volume-reduction surgery. There are also end-of-chapter tools such as chapter summaries, detailed topic outlines, new vocabulary lists, study questions that require the student to explain concepts, and objective-type practice tests.

This 11th edition also contains other useful supplementary tools for approaching a complex subject—perhaps for the first time since high school general biology. This edition includes a separate *Student Survival Guide*, a small booklet, written by one of the co-authors, that contains study tips, including "proven techniques" on studying, note-taking, test-taking, and some summaries of physiology concepts. Having taught structure and function courses in 5 respiratory therapy programs over the years, I can say that most of these, both generic and subject-specific, make good sense for students to pursue. Unfortunately, unless the instructor directly incorporates the booklet into the course, the student may set it aside unread and get none of the "brilliant success" it promises. Teachers need to facilitate its use.

The Panorama CD-ROM disk included with the book contains a few supplemental illustrations for each system and some concepts reviewed in the book. I found the illustrations, boxes, and tables in the text to be quite adequate for most students, but the supplemental ones on the disk may strike a chord for younger students now geared toward that multimedia teaching technique. In my opinion, more important on the disk are the practice quizzes that are not included in the text. There aren't many questions offered, so adding more interactive evaluations is one improvement that could be made in the next edition. The Mosby Web site, http://www.harcourthealth.com/MERLIN, is accessible with a Web site pass code that is included with the book. It offers opportunities to hook up with related links that the student would otherwise need considerable on-line time to find. The available *Instructor's Resource Manual and Test Bank* contains, amongst other tools, a battery of test questions and the answers to the study and critical thinking questions at the end of each chapter in the text. The answers to the objective practice tests are given in the text. When looking at the total resources available for using the text in a course, I wonder how many can be employed without the sheer number becoming difficult to manage by both teacher and student. The instructor would need to select the ones appropriate for the particular course setting and the needs and level of the students.

The only learning tool I found misplaced was the "study tips" box that always occurs at the end of the text chapter rather than at the beginning. It would make more sense to present this box along with the learning objectives in the introduction of the chapter, so the student could benefit from the advice while reading the chapter.

One potential difficulty in reviewing an introductory text on a subject as complex as anatomy and physiology is mistakenly applying the same standard for detail that one would expect of a system-specific text such as a review of respiratory or renal anatomy and physiology. Even so, I found some explanations, such as the one on chemoreceptors in the respiratory chapter, to border on being too abbreviated. Also, the authors missed some generic clinical application opportunities, such as that the electrocardiograph can be used to graphically identify fatal arrhythmias in a "code blue."

In general, this is a good example of the modern "textbook" that has been built on the foundation of a successful written text. It is a multimedia resource that, if the students have the time, can serve those with no background as well as those who desire to go beyond a printed text. The issue that educators must address is that undergraduate students are often so time-pressured with school, work, and home responsibilities that available resources may go unnoticed or untouched. We faculty must learn to pull a text like **Structure & Function of the Body** into the total course materials so that the students will engage it and benefit from its many supplemental resources.

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Cardiopulmonary Anatomy and Physiology for Respiratory Care Practitioners. Gregory P Cottrell. Philadelphia: FA Davis. 2001. Soft cover, illustrated, 389 pages plus companion interactive workbook on CD-ROM, $54.95.

It is an understatement to say that knowledge of cardiopulmonary anatomy and physiology is an important part of a respiratory therapist's education. Indeed, knowledge of this discipline is essential for understanding cardiovascular and pulmonary pharmacology and pathophysiology, critical care concepts, and cardiopulmonary diagnostic tests. It is not surprising, therefore, that a considerable number of texts are available on the subject. Gregory Cottrell's **Cardiopulmonary Anatomy and Physiology for Respiratory Care Practitioners** represents another entry into the growing lists of basic science texts that are primarily devoted to respiratory therapists.

The text is divided into 3 units that group chapters as they relate respiratory, cardiovascular, and renal anatomy and physiology. The author uses a variety of techniques to enhance the text. Each chapter begins with a topical outline, a set of learning objectives, and a list of key terms. A brief summary of the important points discussed in the chapter, along with a concise bibliography, concludes each chapter. Highlighted boxes are interspersed throughout the text to provide the reader with additional information on clinical applications and historical perspectives related to cardiopulmonary anatomy and physiology. The illustrations and tables are clear and accurately convey important information related to the subject being discussed. Appendixes include common abbreviations and symbols used in cardiopulmonary physiology, Dubois charts for calculating body surface area, and a glossary of technical terms. The index enables the reader to easily find important topics covered in the text. This textbook includes a CD-ROM that contains an electronic workbook with review questions for students and an instructor's guide. This added feature should provide a useful resource for students and faculty. Faculty adopting this text will also receive a computerized test along with electronic art files.

The material covered in this text is written in a consistent style that presents complex concepts in a clear and concise manner. The author states in the preface that "the information in the book, though of an advanced nature, is still presented as preclinical information." As such, the level of detail presented is appropriate for the intended purpose and audience.

The first unit of the text devotes 15 chapters to the respiratory system. Chapter 1 contains a good overview of the embryologic development of the respiratory system, along with a discussion of the anatomical and physiologic changes that occur in the respiratory function during the transition from intrauterine to extrauterine life. Chapters 2 through 6 present detailed descriptions of the anatomy of the lungs and thorax, including valuable discussions on neural innervations of the tracheobronchial tree and defense of the respiratory system. The chapters on the mechanics of breathing (Chapters 7, 8, and 9) are presented in a traditional manner, beginning with a description of the static and dynamic properties of the lungs and thorax. A chapter on basic pulmonary function tests (ie, spirometry) is then presented to illustrate how these tests are used in the detection of respiratory system mechanical impairments. The remaining 6 chapters in this unit include information on the control of breathing, ventilation, perfusion, and metabolic function of the lung, gas exchange, gas transport, ventilation-perfusion relationships, and the effects of aging on the respiratory system. I found the discussions of each of these topics to be accurate and very well illustrated, particularly the chapter on ventilation-perfusion relationships. The chapter on the effects of aging on the respiratory system provides important information about a respiratory physiology topic that is often understated or completely overlooked in introductory respiratory anatomy and physiology textbooks. My only concern about this section of the book involves the sequencing of topics. Specifically, the chapter on the control of breathing is presented before the concepts of gas exchange, gas transport, and acid-base balance are discussed in detail. Although Cottrell does provide some background information on these subjects within the chapter on the control of breathing, students enrolled in pre-clinical courses may not have adequate information to fully appreciate the importance of that subject matter.

Unit 2 of the book comprises 7 chapters on the anatomy and physiology of the cardiovascular system. The organization of this section follows very closely the layout used in the first section. Chapter 16 provides a functional overview of the embryologic development of the cardiovascular system, including a description of fetal circulation and the postnatal fate of fetal shunts. The remaining 6 chapters in this section are devoted to anatomy of the heart and blood vessels, hemodynamics, and aging and the cardiovascular system. The descriptions of the gross anatomy and electrophysiology of the heart and of the cardiac cycle are concise and fairly easy to follow. The chapter on hemodynamics contains valuable information, but the author chooses to discuss basic physiologic principles on flow, pressure, and resistance after he introduces the reader to hemodynamic principles. For example, he presents calculations of vascular resistance in Chapter 20, "Hemodynamic Measurements," and then presents Poiseuille's law in Chapter 21, "Flow, Pressure and Resistance in Blood Vessels." Coupling these concepts in this manner may be somewhat confusing for a pre-clinical respiratory therapy student.

The final section of the book (Unit 3) contains chapters on renal anatomy and physiology and acid-base balance. The chapter on the renal system provides a concise review of the macroscopic and microscopic anatomy of the kidneys, along with a brief description of the basic principles of filtration, reabsorption, and secretion as they relate to urine formation and the maintenance of fluid and electrolyte balance. The discussions of osmolarity, countercurrent mechanisms, and hormonal factors influencing urine formation are well organized and easy to follow. The chapter on acid-base balance contains information essential for every respiratory therapist. The author does a good job describing the basic principles of acid-base chemistry, as well as the interaction of renal and respiratory compensatory mechanisms in the maintenance of acid-base homeostasis. Considering the importance of the material covered in this final unit, I believe that this information would serve the reader better if presented earlier in the text.

Overall, I found that this text could be a useful resource for pre-clinical respiratory care students. The author presents many complex topics in a manner that students should find readable and interesting. The pedagogical aids provided encourage students to become proficient in the subject matter before moving on to the next topic. Although respiratory therapy faculty using this text for pre-clinical students can choose to present the subject matter in a "cover-to-cover" approach, the book does allow instructors to use alternative approaches that should be just as effective.

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Acute Lung Injury: From Inflammation to Repair. Geoffrey J Bellingan and Geoffrey J Laurent, Editors. (Biomedical and Health Research Series, Volume 34). Amsterdam: IOS Press. 2000. Hard cover, illustrated, 143 pages, $94.

Acute Lung Injury: From Inflammation to Repair consists of 11 brief yet comprehensive chapters covering the molecular mechanisms of inflammatory lung disease. Particular emphasis is given to the molecular events associated with acute respiratory distress syndrome (ARDS), chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, and oxygen toxicity. Readers interested in a rapid, updated overview of lung molecular biology will find this book most helpful.

The book derives from a symposium on molecular biology given by some of the top leaders in that field. It begins with an introduction to acute lung injury, which, quite appropriately, is mostly clinical, covering the definitions of acute lung injury and ARDS, the epidemiological importance of those syndromes, and their outcomes. This chapter ends with a brief paragraph discussing how advances in basic science described later in the book relate to the clinical arena. The second chapter, "Mechanisms of Inflammation," serves as an introduction to the molecular biology of acute lung injury. The authors discuss the cells involved in acute lung injury, the main pro-inflammatory and anti-inflammatory pathways, and the mechanisms of resolution of inflammation and repair. Taken together, these 2 chapters summarize an incredibly complex topic in a very clear and concise way, providing an ideal introduction to acute lung injury. Respiratory therapists, nurses, and physicians becoming involved in clinical trials investigating molecular pathways of acute lung injury, and who are not familiar with molecular biology, will find these 2 chapters extremely useful.

The remaining chapters provide a more in-depth review of selected topics, loosely divided into 2 sections. The first section is dedicated to mechanisms of inflammation, whereas the second section discusses mechanisms of repair. These 2 sections are separated by a chapter discussing the role of transgenic and knockout mice in the study of lung inflammation and repair. These chapters will be more helpful to people with a particular research interest in the field, who have a minimal background knowledge of molecular biology, or who wish a brief update on recent findings. Pulmonary fellows, post-doctoral students, or research technicians may find these chapters useful as an initial approach to the specific topics discussed.

The section on mechanisms of inflammation begins with an excellent discussion of nitric oxide in acute inflammation, including the current status of therapeutic trials employing inhibitors of nitric oxide synthase in the treatment of septic shock. This is followed by a chapter on macrophage inhibitory factor, a cytokine that has received substantial attention recently as a potential regulator of the effects of glucocorticoids during acute inflammation. The next chapter discusses evidence supporting the hypothesis that an imbalance in lung oxidants and antioxidants is key in the pathogenesis of COPD, as well as the potential roles of antioxidant therapy in the treatment of COPD. Next, the role of neutrophils in acute and chronic lung disease is thoroughly reviewed in a chapter discussing the dynamics of neutrophil recruitment and migration, as well as the current evidence suggesting a key role for neutrophils in the pathogenesis of tissue injury during inflammatory lung diseases. The section on mechanisms of inflammation closes with a discussion on control of inflammation by induction of tolerance, which is well written but targeted more toward T-cell-mediated allergic diseases than toward neutrophilic lung diseases such as ARDS.

The section on mechanisms of lung repair begins with a chapter reviewing the fibroproliferative response to acute lung injury. This chapter discusses both the cells involved in fibroproliferation and the soluble mediators that modulate fibroproliferative responses. The following chapter discusses the multiple roles of thrombin in acute lung injury, with emphasis on its pro-fibrotic effects. The section closes with a chapter on proteases and antiproteases. In all of these chapters the authors discuss the relevance of the laboratory findings to specific clinical entities such as ARDS and COPD.

It should be noted that, because the chapters are derived from oral presentations, they vary widely in readability and clarity. Though most are delightful to read, a few are rather arduous. The reader should be warned that the contents of this book refer to several inflammatory diseases other than acute lung injury, and some aspects of inflammation are discussed solely in the context of these other diseases—something not suggested by the book's title. For example, the chapter on oxidative stress in COPD is very well written and informative, but, considering the title of the book, I would have expected a more thorough discussion of the role on reactive oxygen species in acute lung injury and ARDS.

The book is nicely presented. Some of the chapters have abstracts, but most do not. The book contains abundant typographical errors: for example, the word "interleukin" is spelled "interluekin" at least 4 times. However, my main criticism of the book's presentation is that many of the illustrations are difficult to interpret. Some appear to be black-and-white copies of color images, and the change from color to a gray-scale resulted in a substantial loss of quality and readability. This is unfortunate, as some of the illustrations were probably very useful in the color originals.

In summary, **Acute Lung Injury: From Inflammation to Repair** is a well updated review of the main molecular pathways and mechanisms involved in lung disease. Technicians, respiratory therapists, nurses, and physicians involved in lung research and interested in an overview of the molecular biology of inflammatory lung diseases will find a useful introduction to the topic in this book.

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Lung Surfactants: Basic Science and Clinical Applications. Robert H Notter. (Lung Biology in Health and Disease, Volume 149, Claude Lenfant, Executive Editor.) New York: Marcel Dekker. 2000. Hard cover, illustrated, 444 pages, $150.

This book is number 149 in the Lung Biology in Health and Disease series about all aspects of the lung, with Claude Lenfant from the National Institutes of Health's National Heart, Lung, and Blood Institute as Executive Editor. All the other volumes in the series have been multi-author and focused primarily on research topics or the research basis for clinical problems. This book is the first in this series written entirely by one author, Dr Notter, who states as his goal to create a text where the didactic material relating to interfacial phenomenon and the biophysics of surfactant are brought together for physicians and basic scientists. A strength of the book is that Dr Notter sticks to his basic theme with a consistency and uniformity not possible with multi-author books. On the other hand, the focus on interfacial properties of surfactant, which is Dr Notter's strong suit, results in other aspects of the complex functions of surfactant being less well presented. For example, surfactant metabolism and host defense functions of surfactant are incompletely developed.

The major value of the book for those interested in surfactant is in the first 4 chapters, which build the concepts of interfacial biophysics from the basics to the complex interactions that occur in the alveolus. These chapters have nice simplified conceptual figures of concepts that are foreign to most in the field of pulmonary medicine and respiratory care. A particularly attractive aspect of the book is the inclusion of boxes, throughout the text, in which the critical points are summarized. The casual reader will also appreciate that some of the more technical material, such as thermodynamic analyses of surface pressures, have been set off in smaller type and are thus easily skipped. The text on surface behavior does a good job of summarizing what is known in the field, though these sections and the book as a whole do not present many of the uncertainties and unknowns about how the surfactant system works. For example, the small aggregate forms of surfactant do not contain any of the surfactant proteins and it is not clear how the lipids separate from the proteins during the "life cycle" of alveolar surfactant. More information about the anatomy of the surface film would be helpful to the general reader. A disappointment was the lack of in-depth discussion of the results from some of the new approaches to studying surfactant behavior that suggests "lakes" of different surfactant components.

The book starts with the basics of surface biophysics and ends with the clinical applications of surfactant. The text mixes material in a traditional textbook format, with outlines of protocols for isolations of surfactant, and brief descriptions of surfactant treatment responses in animals. This mixture of formats is somewhat disconcerting. The protocol outlines are a bit like "Methods in Enzymology" but with sufficient detail to only provide the reader with an impression about how to do an alveolar lavage and recover surfactant or how to isolate lamellar bodies from lung homogenates. Similarly, the vignettes describing the responses of animals to surfactant give the reader a flavor of how the experiments were done and what the results were, but there is no attempt to integrate this large literature into a concise overview. At one level, the detail about the surfactant proteins is excessive by providing amino acid sequences in tables. However, clear interpretations about how these proteins function and interact are lacking. For example, there is minimal discussion of the effects of the lack of or overexpression of surfactant proteins in transgenic mouse models. Most of the information about the functions of the surfactant proteins emphasizes biophysical effects and the large amount of information derived from animal models about how these proteins work is abbreviated.

The chapter on lung surfactant dysfunction is a very complete description of what *can* happen to surfactant, based on multiple factors that can influence function. But the reader is left with no sense of what *does* happen. A summary of how these multiple interactions might occur would be helpful for perspective. The approach of listing the possibilities without interpretation continues in the clinical chapters, which describe the complicated pathophysiologies of respiratory distress syndrome and acute respiratory distress syndrome without an attempt to interpret for the reader which surface biophysical principles apply.

The clinical chapters also suffer somewhat because the most recent references are from 1998. For example, in several places in the text surfactants such as Exosurf used to treat respiratory distress syndrome are described, but Exosurf is no longer available in the United States, and ALEC (artificial lung-expanding compound) is no longer distributed in England. There are other surfactants made for clinical use in several developing countries that also are not listed. The inevitable fate for a medical book is that it will be dated as soon as it appears, and studies of surfactant are advancing rapidly, primarily because of transgenic technology. The reviews of the clinical trials of respiratory distress syndrome are adequate for the general reader but continually updated summary analyses by the Cochrane Collaboration are readily available on-line and are a better source for this information.

Overall, the book is accurate and well prepared. The book is of value primarily to people interested in surfactant and who want an in-depth presentation of the biophysical effects of surfactant. This is not a text describing how surfactants can be used clinically. Consequently it will have a relatively narrow audience of clinicians and investigators interested in lung mechanics and surfactant. Minor errors, such as the statement that the human lung is alveolarized by 26 weeks (alveolarization does not occur until about week 32) result from this being a single-author book with material outside Dr Notter's primary subject of expertise. Several references cited in the text are not to the correct reference, but the reference list, with 1,231 items, will be helpful to those working in the field. The index is adequate.

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Cytokines in Pulmonary Disease: Infection and Inflammation. Steve Nelson MD and Thomas R Martin MD, Editors (Lung Biology in Health and Disease, Volume 141, Claude Lenfant, Executive Editor.) New York: Marcel Dekker. 2000. Hard cover, illustrated, 598 pages, $195.

Cytokines in Pulmonary Disease: Infection and Inflammation is another excellent contribution to the Lung Biology in Health and Disease series edited by Claude Lenfant and published by Marcel Dekker. The volume includes excellent reviews of fundamental concepts that the nonimmunologist is likely to find highly appealing. These include an overall introduction to the role of cytokines in anti-microbial defense (written by Galen Toews), a description of cytokine networks and leukocyte recruitment (written by Steve Kunkel et al), a discussion of Th-1 and Th-2 responses (written by Anthony O'Regan and David Center), and a discussion of resolution of inflammation (written by Jason Kelley). The chapter on the use of transgenic mice (written by David Lewis) is likely to be particularly useful, as it clearly describes both the power and limitations inherent in using genetically manipulated mice for exploring immunologic function and provides clear examples relevant to infectious lung diseases. Subsequent chapters present in detail the role of cytokines in the pathophysiology of specific infections. The chapters on tuberculosis (written by Peter Barnes) and on nontuberculous mycobacteria (written by Felix Sangari and Luiz Bermudez) are likely to be of considerable interest both to the pulmonary clinician and to the immunologist. These chapters make it clear that mycobacteriology is a rapidly advancing field at the current cutting edge of immunological science. The role of cytokines in anti-bacterial defense is discussed by co-editor Steve Nelson et al and is a rather broader topic than that covered in other, more specific chapters. Despite this broad mandate, the role of several specific cytokines in antibacterial defense is clearly delineated, providing information that is likely to be useful both to the clinician wishing to understand the heterogeneous nature of responses to infection and to the researcher. The chapter on viral infections (written by Lois Geist and Gary Hunninghake) has a similar broad mandate and focuses on viruses and gene activation. Cytomegalovirus and respiratory syncytial virus are the focus of the chapter. The subject of host response to viruses, however, is rapidly advancing. Some discussion of adenovirus, which is widely used as a vector for gene transfer but can both induce inflammation and cause chronic infection, might have been useful but would probably have exceeded the space provided.

This volume does not address in detail the noninfectious lung diseases often discussed in the context of cytokine biology in the lung, such as the interstitial lung diseases, asthma, or chronic obstructive pulmonary disease. There are chapters, however, that address cytokines in pleural disease (written by Veena Antony and Kamal Abdul Mohammed), in cystic fibrosis (written by Robert Willmott), and in pulmonary transplantation (written by Si Pham et al). The volume, therefore, is accurately described by its subtitle "Infection and Inflammation," although I would have enjoyed a chapter on the role of infection in modulating the cytokine milieu in asthma and chronic obstructive pulmonary disease.

The chapter on extrapulmonary sepsis and cytokines (written by the co-editor Thomas Martin et al) is one of the longer chapters, as might be expected from its clinical importance and with the potential for anti-cytokine therapy. Neither the clinician nor the basic scientist will be disappointed in the exposition provided. The final chapters on gene therapy and host defense continue the overall theme of the volume, presenting cytokine biology as it relates to infectious clinical problems in pulmonary medicine.

The volume, therefore, will be a useful reference for the academic pulmonologist, for the immunologist interested in lung infections, and for the clinician wishing to keep up to date on the basic science relevant to common clinical problems.

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Pulmonary and Peripheral Gas Exchange in Health and Disease. Josep Roca, Roberto Rodriguez-Roisin, and Peter D Wagner, Editors. (Lung Biology in Health and Disease, Volume 148, Claude Lenfant, Executive Editor.) New York: Marcel Dekker. 2000. Hard cover, illustrated, 822 pages, $165.

When I was first asked to review this book I questioned whether it should be reviewed by a pulmonologist or a doctorally prepared physiologist rather than a respiratory therapist. In response, I was asked to provide a review of the book in light of the needs and interests of respiratory therapists. Indeed, interested respiratory therapists could gain a great deal by delving into this book. On occasion, respiratory therapists are maligned because we tend to focus narrowly on "the lung," rather than looking at the broader scope of the entire being. Dr Claude Lenfant's preface to the book touches on this scope as follows: "The overarching theme of this book is therefore to take gas exchange to this integrated level—to better understand how abnormalities in any one organ's ability to transport and utilize oxygen affect the function and oxygen exchange characteristics of the other organs."

This monograph is volume 148 in the Lung Biology in Health and Disease series and is produced in association with the National Institutes of Health's Heart, Lung, and Blood Institute. In case you are not familiar with the Lung Biology in Health and Disease series, the format is that international experts in their fields review state of the art information on selected topics in a succinct fashion for each chapter. To a reader this appears to be a truly daunting task, particularly with the tremendous amount of published research. In fact, a total of 2,374 references to journal articles and textbooks are cited in this volume. Of course, the value of such a work lies not just in the number of citations. The authors critically read the literature, synthesize the findings, describe shortcomings of studies, reveal conflicting study results, and examine continuing controversies. In addition, the authors provide historical perspective on work in their subjects of expertise, where appropriate.

The book is in 4 parts: "Basic Principles," "Pulmonary Gas Exchange," "Gas Exchange in the Periphery: Organs and Systems," and "Integrated Gas Exchange Responses." One might assume that the section on basic principles would merely review information at a level with which respiratory therapists are already fluent based on our education, but that is not the case. The first chapter in this section, "Pulmonary and Peripheral Gas Exchange and Their Interactions," moves very quickly through such information, integrating basic concepts into more comprehensive statements. For instance, one that I found particularly interesting is the expression $D/\beta\dot{Q}$, in which D stands for *diffusional conductance* and relates to Fick's law of diffusion. β encompasses characteristics of the blood's ability to take up oxygen (such as hemoglobin concentration and its position on the oxyhemoglobin curve). $\dot{Q}$ stands for blood flow and its affect on red cell transit time. This treatment of the physiology provides a more comprehensive look at the phenomenon of oxygen uptake in the lung than is provided in the respiratory care texts used in most respiratory therapy programs.

The chapter on "Experimental Approaches to the Study of Gas Exchange" begins with a brief review of measurements with which respiratory therapists will be familiar, such as indirect calorimetry and the Fick principle for determining oxygen consumption. One portion of this chapter deals with the alveolar air equation and efficiency of oxygenation and expands on the equation to reveal limitations in the information it provides regarding the specific causes of oxygenation inefficiency. As one might expect, alveolar ventilation and the efficiency of carbon dioxide elimination are also reviewed. This chapter proceeds to cover techniques used to determine the extent of shunt versus ventilation-perfusion ratio mismatch and the distribution of ventilation and perfusion. Although these techniques are not used clinically (as the chapter's title suggests), the data from studies using these techniques enhance our understanding of ventilation-perfusion matching. One such technique is the multiple inert gas elimination technique (MIGET). MIGET is referred to in virtually every chapter in this book dealing with ventilation-perfusion matching. The author of this chapter provides a brief discussion of this very complicated technique, including several equations that most respiratory therapists would not find meaningful, given our typical level of mathematical preparation. In fact, this chapter is truly not for the mathphobic reader. I believe this chapter is one of the few in this monograph that respiratory therapists will generally not find clinically relevant or educationally valuable, simply because of the level of sophistication required to comprehend the content.

Part 2 contains 8 chapters on pulmonary gas exchange. Topics include "Gas Exchange in Health: Rest, Exercise and Aging," "Altitude and Microgravity," "Anesthesia and Gas Exchange," "Asthma," "Interstitial Lung Diseases," "Pulmonary Vascular Diseases," and "Acute Lung Injury." Each of these chapters is well written and at an appropriate level of difficulty for respiratory therapists to understand, and from which a great deal is to be gained. Once again, these chapters are thorough and contain information that is both historical and current. Although most respiratory therapists do not frequently deal with high altitude nor with microgravity, that chapter, by John West, is interesting, well written, and very readable.

Part 3 is on "Gas Exchange in the Periphery: Organs and Systems." The chapters include: "Whole-Body Oxygen Transport and Use," "Gas Exchange in the Heart," "Localization and Dispersion of Oxygen Demand and Supply in Skeletal Muscle," "The Gut: Oxygen Transport and Gas Exchange Function," "The Brain," and "The Kidney."

Part 4, "Integrated Gas Exchange Responses," comprises 7 chapters: "Pulmonary and Peripheral Gas Exchange During Exercise," "Gas Exchange in Lung and Muscle at High Altitude," "Systemic Gas Exchange and Exercise Performance in Chronic Pulmonary Disease," "Cardiopulmonary and Peripheral Vascular Alterations in Chronic Congestive Heart Failure," "Role of Hemoglobin in the Delivery of Oxygen to Tissues," "Integrated Gas Exchange Response: Chronic Renal Failure," and "Multiple Organ Failure." Understanding these chapters would truly transform the respiratory therapist who only focuses on the lungs into the respiratory therapist who better understands respiration in the whole patient. Anyone who works in critical care has witnessed the relationship between multisystem failure and mortality, and these chapters flesh out the complex interrelationships between the various components of gas exchange and organ failure and describe the bigger picture.

Since this volume is composed of chapters written by numerous contributors, it was not possible to avoid some repetition. Essentially all of the chapters on pulmonary gas exchange refer to the MIGET technique and refer the reader to supplemental sources on the topic, since it is beyond the scope of their specific chapters. In fact, MIGET is referred to far more often than is indicated in the subject index at the end of the book. Although this is repetitious, the findings of MIGET data for each pulmonary disease are different and help to compare and contrast gas exchange limitations in those conditions. Several of the chapters on organs and systems, as well as those on integrated gas exchange responses, describe the controversy regarding pathological dependence of oxygen consumption on oxygen delivery. This is understandable, since each author included this discussion to provide a complete representation of his or her specific topic. Fortunately, this repetition is unlikely to be noticed by most readers, as few will read it cover to cover.

This monograph is sturdily bound, well organized, and generally well edited. Graphs and figures are borrowed from original works and inserted appropriately to complement the text. There are only occasional errors, such as one reference to a "Chapter 27" (there are only 24 chapters). Since the book is composed of chapters written by various authors, it is not surprising to find typographical errors concentrated in the work of a few individuals.

Pulmonary and Peripheral Gas Exchange is in no way an introductory text; rather, it is a book for interested readers with a substantial background in physiology. The chapters on pulmonary gas exchange will increase one's level of understanding of respiration physiology and abnormalities associated with specific disease states. The chapters on extra-pulmonary gas exchange are particularly inviting for respiratory therapists involved in the care of critically ill patients with multisystem failure. This monograph would probably be an excellent reference for respiratory care or physiology faculty in medical schools and for those seeking graduate education in physiology.

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Advanced Respiratory Care (CD-ROM for Microsoft Windows). Robert M Kacmarek PhD RRT FAARC. Philadelphia: Medi-Sim Multimedia/Lippincott Williams & Wilkins. 2000. $1,295.

System Requirements: IBM PC or compatible computer that minimally includes: 486 66 MHz or faster CPU; 8 MB RAM; Windows 95, 98, or NT; SVGA display supporting at least 256 colors; 2X CD-ROM drive; and a Windows-compatible sound card.

Therapeutic outcomes are enhanced by educated clinicians who can appropriately apply and discontinue medical equipment. The goal of every respiratory therapist and intensive care unit clinician should be technical proficiency and consistency in the application of respiratory care modalities. One way to achieve this educational goal would be to send all staff members to the same conference to hear the same presentations and receive the same information from that program. But such simultaneous attendance would be logistically and financially difficult. As an alternative, Dr Kacmarek has put together an educational program in an interactive CD-ROM format. **Advanced Respiratory Care** is a program consisting of pertinent topics presented in a slide format, with illustrative graphs and narration.

Five units are included:

- Weaning from mechanical ventilation
- Noninvasive positive-pressure ventilation in acute respiratory failure
- Innovative approaches to managing acute respiratory failure during mechanical ventilation
- Delivery of aerosolized drugs
- Management of asthma

Each topic (or unit) contains information on a number of interactive screens, a self-test, and a bibliography. A glossary is available in all sections for immediate access to new or review terms. The information is primarily intended for respiratory therapists, but physicians and critical care nurses would also find this information valuable.

The CD-ROM program is said to run on any IBM PC-compatible computer that minimally includes a 486 megahertz or faster CPU, 2X CD-ROM drive, 8 megabytes random access memory, Microsoft Windows (95 or higher), SVGA monitor supporting at least 256 colors, and a Windows-compatible sound card. The program resides in approximately 250 megabytes on the hard drive. There are install options for minimal installation (with which one needs to use the CD-ROM disk to run the program) as well as full installation to the hard drive. No additional hardware or software is required. I installed the program on 3 computers, and it ran without problems on all 3.

Advanced Respiratory Care is an informative though brief review of the topics it presents. The information in each of the 5 units contains references from current studies as well as recommended practices for each of the topics. The content is presented in a slide-type format with no time limit for each slide. The user can determine when to go on to the next slide or back to the previous slide. The 5 topics can be accessed in any order, but each topic must be started from the beginning. Short quizzes are included every 4 or 5 slides, to review the material presented. This has the effect of sharpening one's focus on the material presented, so as to perform well on the quiz. These questions are a mixture of memorization and application of the material presented. This program can be used in the American Association for Respiratory Care's Continuing Respiratory Care Education (CRCE) system for Category 1 credit, when used in a facilitator-guided learning program. Self-instruction does not earn credit.

Although this is a presentation of advanced respiratory care material, there were several errors present. One example was in the unit on aerosol delivery. Here the topic of dry powder inhalers was given several variations, using "drug powder inhaler," "dry powdered inhaler," and "drug powdered inhaler." Twice a slide appeared to be out of order; a new topic was introduced, but the following slide was the quiz for the preceding topic. There is also the occasional quiz question that references information that has not yet been presented.

I had a concern with the section on innovative approaches to managing acute respiratory distress syndrome (ARDS). Dr Kacmarek reviews several techniques for managing ARDS, yet the subject of the ARDS Network's low-tidal-volume protocol for managing ARDS[1] is not included. Is this an oversight? Or is the topic of tidal volume control so well ingrained in ventilator management protocols across the nation and world that the ARDS Network study needs no mention?

The narration added little to the program that couldn't have been better accomplished by clear legends for each graph and picture. The female narrator obviously had no experience (or coaching) with respiratory care, as she mispronounced words in every unit.

On the last self-exam, on management of asthma, it is not possible to obtain a 100% score even if all questions are answered correctly. Better editing in the next version will certainly clear up all those issues.

In the section on noninvasive positive-pressure ventilation in acute respiratory failure, Dr Kacmarek states that his institution is using an intensive care unit ventilator for noninvasive positive-pressure ventilation, but when I last heard Dr Kacmarek speak on noninvasive positive-pressure ventilation, in May 2001, he stated that his primary unit for providing noninvasive positive-pressure ventilation was the Respironics Vision BiPAP machine.

Many areas of respiratory care change quickly. Noninvasive positive-pressure ventilation has seen more (and better) masks every few months. Aerosol delivery devices are introduced often to counter difficulties in actuation, timing, and deposition. New ventilators often introduce interesting new ventilation modes that have not been shown to affect patient outcome. However, studies on advances in ARDS management are not released every 6 months or every year.

What Dr Kacmarek has given us is a new method of presenting current research on respiratory topics. With the multi-media format, this presentation holds one's interest. A department would do well to have all staff required to complete the course on this CD-ROM and provide proof of passing scores.

Altogether, this CD-ROM has promise. The topics are important, up to date, and well referenced (if not completely covered). If there was the availability of updating via the Internet, this CD-ROM would have the prospect of continued value. As offered, it is a tool for a respiratory care department that will provide repeatable, quality, continuing education on important topics. If purchased for a department, this CD-ROM offers an education program that is a good value for its consistency of information (every person is presented with the same information, every time) and for the availability of continuing education units. The advantage for a department of having the staff provide consistent patient care cannot be overemphasized. The price ($1,295) is reasonable when weighed against the cost of conferences and staff time lost attending conferences.

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REFERENCE

1. ARDS Clinical Network, http://hedwig.mgh.harvard.edu/ardsnet. Accessed 11/28/01.

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AARC'S INTERNATIONAL RESPIRATORY CONGRESS

OCTOBER 5-8, 2002

Next year's International Respiratory Congress in Tampa, Florida, promises to offer many unique cultural, educational, and other entertaining experiences to its attendees.

The Tampa Convention Center is located right in the heart of downtown Tampa Bay. The breathtaking waterfront location is conveniently located within walking distance to hotels, restaurants, and clubs. And, after a busy day of lectures, seminars, or classes, trendy shops and galleries are just a hop away.

Come to Tampa, FL, for one of the most breathtaking educational events of the year. Be sure to mark your 2002 calendar for the next AARC Congress, October 5-8, 2002.

TAMPA Bay

American Association for Respiratory Care

MEMBERSHIP APPLICATION

ACTIVE MEMBER

An individual is eligible if he/she lives in the U.S. or its territories or was an Active Member prior to moving outside its borders or territories, and meets ONE of the following criteria (1) is legally credentialed as a respiratory care professional if employed in a state that mandates such, OR (2) is a graduate of an accredited educational program in respiratory care, OR (3) holds a credential issued by the NBRC

ASSOCIATE OR SPECIAL MEMBER

Individuals who hold a position related to respiratory care but do not meet the requirements of Active Member shall be Associate Members They have all the rights and benefits of the Association except to hold office, vote, or serve as chair of a standing committee. The following subclasses of Associate Membership are available Foreign, Physician, and Industrial (individuals whose primary occupation is directly or indirectly devoted to the manufacture, sale, or distribution of respiratory care equipment or supplies) Special Members are those not working in a respiratory care-related field.

STUDENT MEMBER

Individuals will be classified as Student Members if they meet all the requirements for Associate Membership and are enrolled in an educational program in respiratory care accredited by, or in the process of seeking accreditation from, an AARC-recognized agency

SPECIAL NOTICE — Student Members do not receive Continuing Respiratory Care Education (CRCE) transcripts. Upon completion of your respiratory care education, continuing education credits may be pursued upon your reclassification to Active or Associate Member

Please read the eligibility requirements for each of the classifications above, then complete the form. All information requested must be provided, except where indicated as optional. See other side for more information and fee schedule. Please sign and date application on reverse side and type or print clearly. Processing of application takes approximately 15 days.

- ☐ Active
- Associate
  - ☐ Foreign
  - ☐ Physician
  - ☐ Industrial
- ☐ Special
- ☐ Student

Last Name ______________________________

First Name ______________________________

Social Security No. ______________________________

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City ______________________________

State ______________ Zip __ __ __ __ __ - __ __ __ __

Phone No. (________) ______________________________

Work Information:

PLEASE USE THE ADDRESS OF THE LOCATION WHERE YOU PERFORM YOUR JOB, NOT THE CORPORATE HEADQUARTERS IF IT IS LOCATED ELSEWHERE

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City ______________________________
State ______________ Zip __ __ __ __ __ - __ __ __ __
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Preferred Fax No.(________) ______________________________
Preferred Email Address ______________________________
Preferred mailing address: ☐ Home ☐ Business

Would you like to receive our monthly newsletter, AARC Repor by email?
☐ Yes ☐ No

Have you ever been or are you currently in the military?
☐ Yes ☐ No

Demographic Questions (optional)

We request that you answer these questions in order to help us design services and programs to meet your needs.

Primary Job Responsibility (check one only)

- ☐ Director (Technical or Program)
- ☐ Supervisor
- ☐ Diagnostic Technologist
- ☐ Instructor/Educator
- ☐ Other, specify ______________________________
- ☐ Therapist/Technician
- ☐ Medical Director
- ☐ Student
- ☐ Staff Nurse

Type of Business

- ☐ Educational Institution
- ☐ DME/HME
- ☐ Home Health Agency
- ☐ Hospital/Acute Care
- ☐ Other, specify ______________________________
- ☐ Manufacturer or supplier
- ☐ Outpatient Clinic
- ☐ Physician office
- ☐ Skilled Nursing Facility

Check the Highest Degree Earned

- ☐ High School
- ☐ RC Graduate Technician
- ☐ Associate Degree
- ☐ Bachelor's Degree
- ☐ Master's Degree
- ☐ Doctorate Degree

Number of Years in Respiratory Care

- ☐ 0-2 years
- ☐ 3-5 years
- ☐ 6-10 years
- ☐ 11-15 Years
- ☐ 16 years or more

Job Status

- ☐ Full Time
- ☐ Part Time

Credentials

- ☐ RRT
- ☐ CRT
- ☐ Physician
- ☐ CRNA
- ☐ RN
- ☐ LVN/LPN
- ☐ CPFT
- ☐ RPFT
- ☐ Perinatal/Pediatric

Date of Birth ______________ Sex ____________

FOR STUDENT MEMBER – REQUIRED

School/RC Program ______________________________
Address ______________________________
City ______________________________
State ______________ Zip __ __ __ __ __ - __ __ __ __
Phone No. (________) ______________________________

Expected Date of Graduation (REQUIRED INFORMATION)

Month ________ Year ________

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American Association for Respiratory Care **MEMBERSHIP APPLICATION**

Membership Fees

Payment must accompany your application to the AARC. Fees are for 12 months. These fees contain the $12.50 new members processing fee. Renewing members (except students) can deduct $12.50.

CHOOSE ONE LEVEL OF MEMBERSHIP

AARC REGULAR MEMBERSHIP (Receive both AARC Times and Respiratory Care journal)

☐ Active	$102.50
☐ Associate (Industrial or Physician)	$102.50
☐ Associate (Foreign)	$117.50
☐ Special	$102.50
☐ Student	$ 50.00

OR

AARC CHOICE MEMBERSHIP(Choose one publication)

☐ Active	$ 91.00
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☐ Associate (Foreign)	$106.00
☐ Special	$ 91.00

I want ☐ AARC Times ☐ Respiratory Care journal

OR

AARC PLUS MEMBERSHIP (All publications and other items)

☐ Active	$137.50
☐ Associate (Industrial or Physician)	$137.50
☐ Associate (Foreign)	$177.50
☐ Special	$137.50

(Includes one free section - please mark choice below.)

Specialty Sections (optional)

Established to recognize the specialty areas of respiratory care, these sections publish a newsletter four times a year that focuses on issues of specific concern to that specialty. The sections also design the specialty programming at the national AARC meetings.

☐ Adult Acute Care Section	$15.00
☐ Education Section	$20.00
☐ Perinatal-Pediatric Section	$15.00
☐ Diagnostics Section	$15.00
☐ Continuing Care-Rehabilitation Section	$15.00
☐ Management Section	$20.00
☐ Transport Section	$15.00
☐ Home Care Section	$15.00
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PLEASE SIGN

I hereby apply for membership in the American Association for Respiratory Care and have enclosed my dues. If approved for membership in the AARC, I will abide by its bylaws and professional code of ethics. I authorize investigation of all statements contained herein and understand that misrepresentations or omissions of facts called for is cause for rejection or expulsion.

A yearly subscription to Respiratory Care journal and AARC Times magazine includes an allocation of $11.50 from my dues for each of these publications.

NOTE: Contributions or gifts to the AARC are not tax deductible as charitable contributions for income tax purposes. However, they may be tax deductible as ordinary and necessary business expenses subject to restrictions imposed as a result of association lobbying activities. The AARC estimates that the nondeductible portion of your dues — the portion which is allocable to lobbying — is 26%.

Signature ____________________

Date ____________________

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TOTAL SECTION FEE $__________

GRAND TOTAL = Membership Fee plus optional sections

$__________

☐ Total Amount Enclosed $__________

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RESPIRATORY CARE

Manuscript Preparation Guide

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Categories of Articles

Research Article: A report of an original investigation (a study). Must include: Title Page, Abstract, Key Words, Introduction, Methods, Results, Discussion, Conclusions, and References. May also include: Tables, Figures (if so, must include Figure Legends), Acknowledgments, and Appendixes.

Review: A comprehensive, critical review of the literature and state-of-the-art summary of a topic that has been the subject of at least 40 published research articles. Must include: Title Page, Outline, Abstract, Key Words, Introduction, Review of the Literature, Summary, and References. May also include: Tables, Figures (if so, must include Figure Legends), Acknowledgments, and Appendixes.

Overview: A critical review of a pertinent topic that has fewer than 40 published research articles. Same structure as Review Article.

Update: A report of subsequent developments in a topic that has been critically reviewed in RESPIRATORY CARE or elsewhere. Same structure as a Review Article.

Special Article: A pertinent paper not fitting one of the other categories. Consult with the Editor before writing or submitting such a paper.

Editorial: A paper addressing an issue in the practice or administration of respiratory care. It may present an opposing opinion, clarify a position, or bring a problem into focus.

Letter: A brief, signed communication responding to an item published in RESPIRATORY CARE or about other pertinent topics. Tables, Figures, and References may be included. The letter should be marked "For Publication."

Case Report: Report of an uncommon clinical case or a new or improved method of management or treatment. A case-managing physician must either be an author or furnish a letter approving the manuscript. Must include: Title Page, Abstract, Key Words, Introduction, Case Summary, Discussion, and References. May also include: Tables, Figures (if so, must include Figure Legends), and Acknowledgments.

Point-of-View: A paper expressing personal but substantiated opinions on a pertinent topic. Must include: Title Page, Text, and References. May also include: Tables and Figures (if so, must include Figure Legends).

Drug Capsule: A miniature review paper about a drug or class of drugs. Drug Capsules address pharmacology, pharmacokinetics, and/or pharmacotherapy.

Graphics Corner: A brief, instructive case report discussing and illustrating waveforms for monitoring or diagnosis. Must include: Questions, Answers, and Discussion.

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Test Your Radiologic Skill: A brief, instructive case report pertinent to respiratory care and involving imaging, including one or more radiographs or other images submitted as black and white glossy photographs that clearly illustrate the teaching points being made. Must include: Questions, Answers, and Discussion.

Preparing the Manuscript

Double-space the text and number the pages. Do *not* include author names, author institutional affiliations, or allusions to institutional affiliations anywhere except on the title page. On the Abstract page include the title but do not include author names. Begin each of the following on a new page: Title Page, Abstract, Text, Acknowledgments, References, each Table, each Figure, and each Appendix. Use standard English in the first person and active voice. Type all headings in initial-capital letters (eg, Introduction, Methods, Patients, Equipment, Statistical Analysis, Results, Discussion). Center the main section headings and place second-level headings on the left margin.

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Paper accepted but not yet published:
Hess D. New therapies for asthma. Respir Care (year, in press).

Article in a journal carrying pagination throughout the volume:
Legere BM, Kavuru MS. Pulmonary function in obesity. Respir Care 2000;45(8):967-968.

Article in a publication that numbers each issue beginning with Page 1:
Kallstrom TJ. Focus on asthma—disease management: a role for the respiratory therapist. AARC Times 1999;23(Oct):16, 17, 19.

Corporate author journal article:
American Association for Respiratory Care. Clinical Practice Guideline. Removal of the endotracheal tube. Respir Care 1999;44(1):85-90.

Article in journal supplement: (Journals differ in numbering and identifying supplements. Supply information sufficient to allow retrieval.)
Barnes PJ. Endogenous inhibitory mechanisms in asthma. Am J Respir Crit Care Med 2000; 161(3 Pt 2):S176-S181.

Abstract in journal: (Abstracts citations are to be avoided, and those more than 3 years old should not be cited.)
Volsko TA, De Fiore J, Chatburn RL. Acapella vs flutter: performance comparison (abstract). Respir Care 2000;45(8):991.

Editorial in a journal:
Giordano SP. What's that sound? (editorial) Respir Care 2000;45(10):1167-1168.

Editorial with no author given:
The perils of paediatric research (editorial). Lancet 1999;353(9154):685.

Letter in journal:
Piper SD. Testing conditions for nebulizers (letter). Respir Care 2000;45(8):971.

Book: (For any book, specific pages should be cited whenever reference is made to specific statements or other content.)
Cairo JM, Pilbeam SP. Mosby's respiratory care equipment, 6th ed. St Louis: Mosby; 1999:76-85.

Corporate author book:
American Medical Association Department of Drugs. AMA drug evaluations, 3rd ed. Littleton CO: Publishing Sciences Group; 1977.

Chapter in book with editor(s):
Isono S. Upper airway muscle function during sleep. In: Loughlin GM, Carroll JL, Marcus CL, editors. Sleep and breathing in children: a developmental approach. (Lung Biology in Health and Disease, Vol 147, Claude Lenfant, Executive Editor.) New York/Basel: Marcel Dekker; 2000:261-291.

World Wide Web
American Lung Association. Trends in pneumonia, influenza, and acute respiratory conditions mortality and morbidity. February, 2000. http://www.lungusa.org/data. Accessed November 20, 2000.

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call for abstracts

RESPIRATORY CARE • OPEN FORUM 2002

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The American Association for Respiratory Care and its science journal, RESPIRATORY CARE, invite submission of brief abstracts related to any aspect of cardiorespiratory care. The abstracts will be reviewed, and selected authors will be invited to present posters at the OPEN FORUM during the AARC International Respiratory Congress in Tampa, Florida, October 5-8, 2002. Accepted abstracts will be published in the August 2002 issue of RESPIRATORY CARE. Membership in the AARC is not required for participation. All accepted abstracts are automatically considered for ARCF research grants.

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MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For VOLUNTARY reporting
by health professionals of adverse
events and product problems

Page ____ of ____

Form Approved OMB No. 0910-0291 Expire
See OMB statement o

FDA Use Only (Resp Care)

Triage unit
sequence #

A. Patient information

1 **Patient identifier**

In confidence

2 **Age at time of event:**

or

Date of birth:

3 **Sex**

☐ female

☐ male

4 **Weight**

____ lbs

or

____ kgs

B. Adverse event or product problem

1 ☐ **Adverse event** and/or ☐ **Product problem** (e.g., defects/malfunctions)

2 **Outcomes attributed to adverse event** (check all that apply)

☐ death ____ (mo/day/yr)

☐ life-threatening

☐ hospitalization – initial or prolonged

☐ disability

☐ congenital anomaly

☐ required intervention to prevent permanent impairment/damage

☐ other: ____

3 **Date of event** (mo/day/yr)

4 **Date of this report** (mo/day/yr)

5 **Describe event or problem**

6 **Relevant tests/laboratory data,** including dates

7 **Other relevant history, including preexisting medical conditions** (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

C. Suspect medication(s)

1. **Name** (give labeled strength & mfr/labeler, if known)

#1

#2

2 **Dose, frequency & route used**

#1

#2

3 **Therapy dates** (if unknown, give dura
from/to (or best estimate)

#1

#2

4 **Diagnosis for use** (indication)

#1

#2

5. **Event abated after u stopped or dose red**

#1 ☐ yes ☐ no ☐

#2 ☐ yes ☐ no ☐

6 **Lot #** (if known)

#1

#2

7. **Exp. date** (if known)

#1

#2

8. **Event reappeared a reintroduction**

#1 ☐ yes ☐ no ☐

#2 ☐ yes ☐ no ☐

9 **NDC #** (for product problems only)

– –

10. **Concomitant medical products** and therapy dates (exclude treatment of even

D. Suspect medical device

1 **Brand name**

2. **Type of device**

3 **Manufacturer name & address**

4 **Operator of devi**

☐ health profess

☐ lay user/patie

☐ other:

5. **Expiration date** (mo/day/yr)

6

model # ____

catalog # ____

serial # ____

lot # ____

other #

7 **If implanted, giv** (mo/day/yr)

8 **If explanted, giv** (mo/day/yr)

9 **Device available for evaluation?** (Do not send to FDA)

☐ yes ☐ no ☐ returned to manufacturer on ____ (mo/day/yr)

10. **Concomitant medical products** and therapy dates (exclude treatment of even

E. Reporter (see confidentiality section on back)

1 **Name & address**

phone #

2. **Health professional?**

☐ yes ☐ no

3. **Occupation**

4 **Also reported to**

☐ manufacturer

☐ user facility

☐ distributor

5 If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☐

FDA

Mail to: MEDWATCH
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or FAX to:
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FDA Form 3500 1/96)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the ev

ADVICE ABOUT VOLUNTARY REPORTING

Report experiences with:

- medications (drugs or biologics)
- medical devices (including in-vitro diagnostics)
- special nutritional products (dietary supplements, medical foods, infant formulas)
- other products regulated by FDA

Report SERIOUS adverse events. An event is serious when the patient outcome is:

- death
- life-threatening (real risk of dying)
- hospitalization (initial or prolonged)
- disability (significant, persistent or permanent)
- congenital anomaly
- required intervention to prevent permanent impairment or damage

Report even if:

- you're not certain the product caused the event
- you don't have all the details

Report product problems – quality, performance or safety concerns such as:

- suspected contamination
- questionable stability
- defective components
- poor packaging or labeling
- therapeutic failures

How to report:

- just fill in the sections that apply to your report
- use section C for all products except medical devices
- attach additional blank pages if needed
- use a separate form for each patient
- report either to FDA or the manufacturer (or both)

Important numbers:

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• 1-800-FDA-7737	to report by modem
• 1-800-FDA-1088	to report by phone or for more information
• 1-800-822-7967	for a VAERS form for vaccines

If your report involves a serious adverse event with a device and it occurred in a facility outside a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

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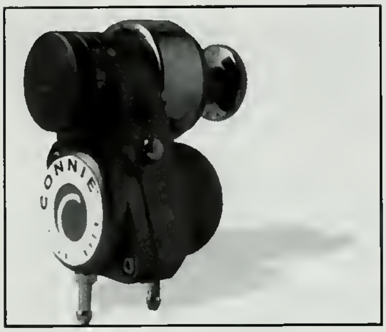
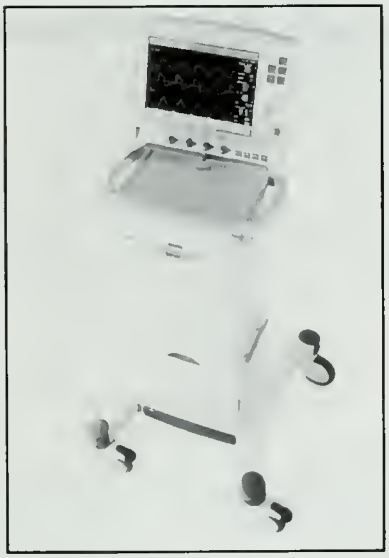
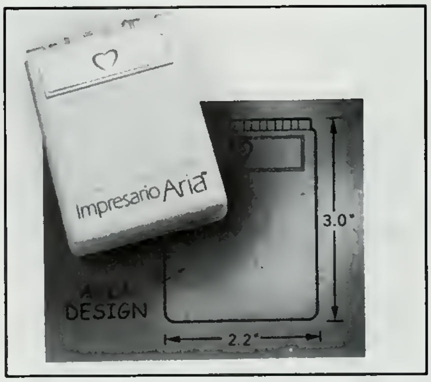


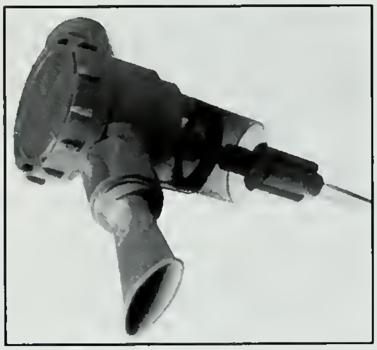
Oxygen Conserver. HME Technologies introduces the Connie O$_2$ Conserver. The manufacturer says that this new oxygen conserver is designed for medium- and low-pressure liquid oxygen delivery systems and when placed on an oxygen reservoir utilizes twice as much oxygen out of every liquid oxygen tank. For more information from HME Technologies, circle number 197 on the reader service card in this issue, or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/.



Ventilator Platform. The Electromedical Systems Division of Siemens Medical Solutions USA, Inc has introduced to the U.S. market what they describe as "a comprehensive new ventilator platform, Servo^i, to bring to the user enhanced levels of clinical performance, cost efficiency and mobility." Servo^i provides a single ventilator that can be customized to treat all categories of patients, from neonate through pediatric to adult, according to the manufacturer. They also say that this new product provides tools needed in different treatment methodologies plus a wide range of ventilation modes such as enhanced volume support, SIMV-PRVC and Automode® function and that the simple and easy to use interface allows users to become readily familiar with the aesthetic design and control layout. The Servo^i comes in three system configurations—the Servo^i Infant, Servo^i Adult, and Servo^i Universal. For more information from Siemens, circle number 198 on the reader service card in this issue, or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/



Digital ECG Recorder. Del Mar Medical Systems has introduced its newly enhanced digital Holter recorder, Aria. The latest version of this pager-sized Holter recorder can record and store 48 hours of uncompressed ECG data in non-volatile memory, according to Del Mar. The manufacturer also claims that it can be optionally configured to detect and record pacemaker activity for analysis on Del Mar's Holter scanners. This recorder is 3.0 by 2.2 inches and weighs 3 ounces. It uses 4 leads to record 3 channels of patient ECG data. Its features include (according to the manufacturer) auto-calibration, patient event-recording capability, an audible tone and LED to confirm recording, and is powered by one AA alkaline or rechargeable battery. For more information from Del Mar Medical Systems, circle number 199 on the reader service card in this issue, or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/



Reusable Nebulizer. Respironics HealthScan Asthma & Allergy Products introduces the new Ventstream Reusable High Efficiency Nebulizer. According to Respironics, the Ventstream provides fast, targeted delivery of aerosol medications. The manufacturer claims that 80% of Ventstream's aerosol output falls below 5.0 microns, and that its unique jet design produces an aerosol with an MMAD of 3.0 microns. For more information from Respironics, circle number 200 on the reader service card in this issue, or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

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Scheduled Professor's Rounds 2002

Withholding and Withdrawing Life Support in the ICU — Gordon D Rubenfeld MD / Richard D Branson BA RRT FAARC — Live February 12; Audio March 5

Weaning from Mechanical Ventilation: New Insights, New Guidelines — Neil R MacIntyre MD FAARC/ Dean R Hess PhD RRT FAARC — Live April 16; Audio May 14

Neonatal and Pediatric Ventilators: What's the Difference? — Mark J Heulitt MD FAARC/ Richard D Branson BA RRT FAARC — Live May 21; Audio June 25

Ventilator Graphs: What's With That Wave? — Jon O Nilsestuen PhD RRT FAARC/ Richard D Branson BA RRT FAARC —Live July 16; Audio August 13

Talking with Patients and Families About Death and Dying— Helen M Sorensen MA RRT FAARC/ David J Pierson MD FAARC —Live August 20; Audio September 17

Pressure vs Volume Ventilation: Does It Matter? — Robert S Campbell RRT FAARC/ Richard D Branson BA RRT FAARC — Live September 10/ Audio October 8

Inpatient Management of COPD — Randall Rosenblatt MD/ David J Pierson MD FAARC — Live October 22; Audio November 12

High-Frequency Oscillatory Ventilation — Thomas E Stewart MD/ Richard D Branson BA RRT FAARC — Live November 19; Audio December 10

Helpful Web Sites

American Association for Respiratory Care
http://www.aarc.org
- Current job listings
- American Respiratory Care Foundation fellowships, grants, & awards
- Clinical Practice Guidelines

National Board for Respiratory Care
http://www.nbrc.org

RESPIRATORY CARE online
http://www.rcjournal.com
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- Contact the editorial staff
- OPEN FORUM; submit your abstract online

Asthma Management Model System
http://www.nhlbi.nih.gov

Keys to Professional Excellence
http://www.aarc.org/keys/

Committee on Accreditation for Respiratory Care
http://www.coarc.com

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CPFT	$200 (new applicant) $170 (reapplicant)
RPFT	$250 (new applicant) $220 (reapplicant)
RRT (Written & CSE)	$190 (new) $150 (reapplicant) written only $200 (new and reapplicant) CSE only $390 (new) $350 (reapplicant) both

For information about other services or fees, write to the National Board for Respiratory Care,
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or e-mail: nbrc-info@nbrc.org

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Calendar of Events

Date	AARC & State Society Programs	Contact
March 13–15	Greater Bay Area Chapter of the CSRC's 23rd Annual Tahoe Conference; **Lake Tahoe, CA**	California Society for Respiratory Care, (925) 866-6643, (925) 947-4487, or www.csrc.org
March 21-23	Tennessee Society's State Meeting; **Franklin, TN**	Patti Joiner, pjoyner@mmcc-tlc.com
April 2-4	Rhode Island Society's Annual Convention & Seminar; **Newport, RI**	Wayne Foresti, (401) 769-8758 or RIWPF732@aol.com
April 4	TSRC North Region – Pineywoods District 16th Annual Spring Seminar; **Lufkin, TX**	Pam Hollis (409) 639-7006
April 4–5	Alabama Society for Respiratory Care Clinical Conference at the Beach; **Gulf Shores, AL**	Bill Pruitt (251) 434-3405 or wpruitt@jaguar1.usouthal.edu
April 10–12	44th Annual MSRC Seminar; **Pontiac, MI**	Annie Hurlburt (734) 677-MSRC or ahurlburt@ucia2.
April 11–12	PSRC 5th Annual Eastern Regional Conference & Exhibition; **King of Prussia, PA**	Ann Cusano (215) 646-7300, ext. 428 or cusano.a@gmc.edu
April 19	TSRC North Region – Friendship District & Huguley Medical Center, Pediatric/Neonatal; **Fort Worth, TX**	Joe Horn (817) 551-2766
April 25–26	TSRC Northwest Region "Spring Training"; **Lubbock, TX**	Karen Spann (806) 351-1600, ext. 305
April 28–29	29th Annual Pacific NW Regional Respiratory Care Conference; **Bellevue, WA**	Ellen Perry (425) 576-1171 or ezperry@earthlink.net
May 2–3	TSRC's Central Region – Rio Grande Valley District Seminar; **South Padre Island, TX**	John Galan (956) 969-5185
May 7–8	CSRC 20th Annual Super Symposium; **Southington, CT**	Sue Albino (860) 545-2414 or salbino@harthosp.org
May 13–15	MSRC's Annual Spring Fling, **Lewiston, ME**	Diane Haskell (207) 596-8872 or Dhaskell@nehealth.org; Bobbie Crockett (207) 262-2214 or roberta.crockett@sjhhealth.com; www.mesrc.org
June 14–16	AARC Summer Forum; **Vail, CO**	AARC, (972) 243-2272, www.aarc.org
June 16–17	AARC Asthma Disease Management Course; **Vail, CO**	AARC, (972) 243-2272, www.aarc.org
July 17–19	TSRC 31st Annual Convention and Exhibition; **San Antonio, TX**	TSRC Executive Office (972) 680-2455
Sept. 5–7	TSRC North Region – Pineywoods District 16th Annual Fall Seminar; **Lufkin, TX**	Pam Hollis (409) 639-7006
Sept. 12–13	Alabama Society for Respiratory Care Annual Meeting; **Birmingham, AL**	Bill Pruitt (251) 434-3405 or wpruitt@jaguar1.usouthal.edu
Oct. 5–8	AARC 48th International Respiratory Congress; **Tampa, FL**	AARC, (972) 243-2272, www.aarc.org

Date	Other Meetings	Contact
March 8	Alfred I. duPont Hospital for Children meeting: High Frequency Oscillatory Ventilation Pediatric Application; **Wilmington, DE**	Sally N. Levine (302) 651-6758 or snlevine@nemour
March 12–13	Practical Spirometry Course; **Rochester, MN**	Mayo Pulmonary Services, Mayo Clinic, (800) 533-1
April 6–8	Washington Regional Medical System's Spring Sleep Seminar 2002 and APT Basic Course; **Memphis, TN**	Bill Rivers or Melinda Trimble, (501) 713-1272, brivers@wregional.com, or mtrimble@wregional.cor
April 16–19	All Children's Hospital: Neonatal/Pediatric Transport Conference; **St. Petersburg, FL**	Connie Spadaccino (800) 456-4543, ext. 4240
April 18–20	University of California San Francisco's Antiviral Chemotherapy; **San Francisco, CA**	Department of Medicine (415) 476-5208
April 25–27	2nd annual FOCUS on Respiratory Care and Sleep Medicine Conference: **St. Louis, MO**	Bob Miglino (800) 661-5690 or www.foocus.com

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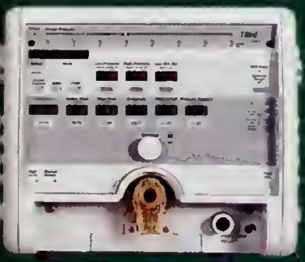

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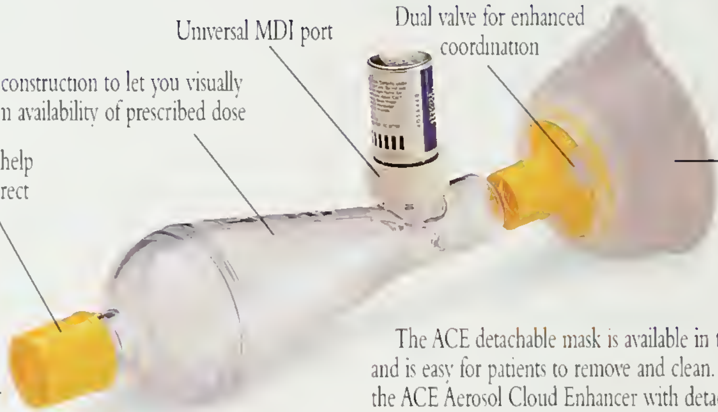
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